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THE QUARTERLY REVIEW of BIOLOGY

CELL DIVISION
PART ONE
A THEORETICAL APPROACH TO THE PRIMEVAL MECHANISM, THE INITIATION OF CELL DIVISION, AND CHROMOSOMAL CONDENSATION

BY NORMAN G. ANDERSON

Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee

"Regarding fear of hypotheses, all that need be said is this: the only hypotheses we need be afraid of are those which do not have testable consequences."

J. H. Woodger, 1948

INTRODUCTION

THE present series of papers represents a frank attempt made during the past five years to formulate a detailed theoretical approach to the problem of cell division. In the past a number of theories relating to mitotic events have been put forward. The more plausible of these have been critically reviewed by Schrader (1953). None of these appear to have served the functions of a scientific theory, which are first to suggest fruitful experiments that would not otherwise have been done, and second to indicate crucial experiments that will either support or destroy the theory itself. No general review will be presented here.

The point of view to be adopted here is that mitosis, as seen in contemporary plants and animals, includes many different refinements and modifications of one simple ancient mechanism operative in the first living cells. This view is in contrast to that presented by Schrader (1953), who does not consider that one underlying common denominator exists, but rather that ". . . mitosis is comprised of a great complex of different mechanisms." The nature and course of development of a proposed primeval process will be discussed in some detail before attempting to show its role in modern mitotic events, viz., the initiation of cell division, chromosomal condensation, nuclear envelope and nucleolar dissolution and re-formation, spindle and aster production, chromosomal movement, and the reconstruction of the nucleus.

It is necessary to present a number of topics in considerable detail. Since the thread of the argument is thereby easily lost, a brief summary is presented in the first paragraph of each large section of the paper. Initially, certain fundamental aspects of living systems generally will be considered, since these must form the basis for the postulates on which the theory is based. Space, time, and the limitations of the author's interests of necessity set bounds to the literature surveyed, and direct the choice of works cited.

It is evident that the cell is not an infinitely diverging system (Haurowitz, 1950). Thus, although the synthesis of many simple compounds is accomplished in a stepwise manner by an array of enzymes, the enzymes themselves cannot each

be formed by another array of specific enzymes which in turn are each produced by still another set of specific enzymes. The finite size of the cell limits the number of such sets or generations. Therefore, although at the present time new enzymes and new enzyme systems are constantly being described, so as to result in greater apparent complexity (divergence), there must come a point where convergence in biological systems will become evident. In the present context convergence means multiplicity of function. The cell can only be of finite size if it contains a number of functional entities each of which does more than one thing. Thus, on a simple level, phosphate acceptors in the cell serve a number of specific functions in addition to which, by their varying availability, they control the rates of a great number of enzymatic reactions involved in their synthesis (Potter, Recknagel, and Hurlbert, 1951). All the cell solutes, from the microions, such as potassium and magnesium which have profound effects on certain enzymatic reactions, to the macromolecular enzymes with their well-known specificities, may also be considered as a group of substances which dictate by their concentration the tonicity and certain osmotic properties of the cell. The association of enzymes with "insoluble" cell particulate material (Green, 1952; Schneider and Hogeboom, 1951) suggests that enzyme molecules may be linked together to form the fabric of these structures, and may thus serve at one time both catalytic and structural functions. On a higher level, the very nature of life necessitates the existence of molecules which duplicate themselves by one means or another (autocatalysis) and which engage in some second or third highly specific function in addition to self-duplication (heterocatalysis or structure-building). The gene is a case in point, although multiplicity of function should not be considered as being limited to the nucleus.

The multiplicities of function and interaction of a great number of constituents of the cell, which are here considered to be the essence of a living system, are the bases for the delicate, continuous, internal control which characterizes all living cells. For this reason a number of familiar biological entities, such as nucleic acids and enzymes, may be treated both as molecules possessing great individuality and functional specificity, and as classes of substances engaging in certain other important processes where such simple properties as size, charge, or shape may be the only relevant characteristics. It is from these "secondary" characteristics of protoplasmic constituents that the proposed mechanism will be constructed.

An attempt to describe a complex process such as cell division should avoid postulating the existence of a new substance, plasm, or enzyme for each change or effect observed (Woodger, 1948). Therefore, these discussions will be limited to fairly well-characterized cell constituents. These include nucleic acids and certain general classes of proteins including known enzymes, coenzymes, and salts. The mechanism proposed is based on known properties of these substances. Only when it is found impossible to explain the many aspects of cell division with such known substances, is it justifiable to invoke any of the many hypothetical substances which have been postulated. It goes without saying that much of the terminology of cytological literature, which often includes several dozen names for the same morphological entity, is often of little use in a discussion of cell division on a molecular level. This is especially true of the various "plasms" which have been described.

THE PRIMEVAL MECHANISM

It is proposed that the primeval mechanism, which is thought to underlie present-day mitotic processes, involved a change in the number of polymerized positively or negatively charged groups (a shift in polyelectrolyte balance) in a colloidal system composed predominantly of colloids bearing a net negative charge. The nature and origin of such a mechanism will be discussed in terms of contemporary thought concerning early conditions on the surface of the earth and the origin of life. It will be shown that the composition of the primeval atmosphere and the pH of the primeval seas dictated the nature of the building blocks available and the sign of the charge on the colloids formed, and laid the basis for metabolic systems extracting energy from organic acids in place of organic bases.

It appears to be generally accepted that a rich variety of organic compounds was formed on the earth's surface prior to the advent of life (Haldane, 1933; Oparin, 1938; Holmes, 1948; Lwoff, 1951; Bernal, 1951; Blum, 1951; Urey, 1952). The original experimental work purporting to demonstrate the formation of a vast variety of organic substances when water, carbon dioxide, and ammonia were irradiated with ultraviolet light, which was cited by Haldane (1933), has never been repeated despite numerous attempts, according to van Niel (1949), although Calvin

(1956) claims positive results. However, Miller (1953, 1955) was able to demonstrate the production of a number of amino acids and other organic compounds, by using an electrical discharge in a closed system. Miller used an atmosphere of methane, ammonia, hydrogen, and water as suggested by Oparin (1938), Urey (1952), and Bernal (1951). This experiment has been repeated (Anderson and Tolbert, 1954, unpub.) and at least fourteen ninhydrin-positive substances demonstrated by paper chromatography. Although much experimental work remains to be done, it does not appear unreasonable to assume that the "soup" of organic substances originally proposed by Haldane actually did exist.

It is evident that an ocean covered by an atmosphere containing ammonia must be alkaline. The synthetic system suggested by Urey and Miller then involved a gigantic refluxing process in which organic materials formed in the atmosphere would be constantly settling into the seas. Substances volatile in alkali would be recycled. As a result, fatty acids would accumulate in the seas, while organic bases would be involved in further reactions. As these volatile organic bases were subjected again and again to the ionizing radiations and electrical discharges of the upper air, they were built into more and more complex but also less volatile substances such as amino acids and purine and pyrimidine bases. The system is thus biased precisely in favor of the accumulation of simple acidic substances familiar to us now as metabolic intermediates, the amino acids, and the complex organic bases which are fundamental to the formation of nucleic acids and metal-containing catalysts—i.e., the building blocks for living cells. Further, in an alkaline medium, the most stable colloids would be those bearing a net negative charge.

The formation of compounds of colloidal dimensions, however, is a quite different matter. One of the major difficulties is that the same factors which are thought to have produced the variety of simple compounds originally, tend to destroy nucleic acids and nucleoproteins as well as other organic compounds. Thus proteins are denatured or inactivated by ultraviolet light (reviewed by Schomer, 1936), heat, or ionizing radiations (Svedberg and Brohult, 1939; Barron, 1954), while nucleic acids are depolymerized by similar treatments (Hollaender, Greenstein, and Jenrette, 1941; Sparrow and Rosenfeld, 1946; Taylor, Greenstein, and Hollaender, 1948). Solar radiation includes not only ultraviolet but x-radiation as well (see review by Sanderson and Hulburt, 1954). In the present-day atmosphere oxygen begins to absorb at 2700 Å and removes a large percentage of radiation below this wave length. As a result of this absorption a small amount of ozone is produced. The ultraviolet absorption of ozone, beginning with the Huggins bands between 3400 and 3100 Å and rising sharply below 3100 Å in the so-called Hartley continuum, accounts for the complete absence of radiation between 2150 and 2915 Å on the surface of the earth. If the primeval atmosphere were low in oxygen, as has been suggested, large amounts of short ultraviolet would have reached the surface of the earth. Under such conditions it is necessary to postulate the polymerization of amino acids or nucleotides as occurring either in sands or clays, or under a water blanket.

A second difficulty is that energy is required for the synthesis of either proteins or nucleic acids, a fact making the spontaneous formation of a large polymer to appear as a very unlikely event. The chances of forming a chain of ten amino acids, for example, is given by Blum (1951) as about 10^{-30}. Lanham (1952) avoided this difficulty by proposing that the original proteins were formed from precursors other than simple amino acids. These precursors were presumed to be energy-rich and to condense spontaneously. Only when the environment became depleted of these substrates does Lanham propose that a mechanism for the synthesis of adenosine triphosphate (ATP) or other high-energy compounds was evolved. Blum, on the other hand, suggests that sources of chemical energy such as ATP were present in the environment originally and were used by the first autocatalytic molecules for protein or nucleic acid synthesis, without stating how the first such ATP-utilizing molecule was formed. The instability of ATP in alkaline solutions makes Blum's suggestion highly unlikely.

Two general theories of the original "living" substance have been proposed. These are the coacervate theory (Oparin, 1938) and the nucleoprotein or reduplicating molecule theory (Alexander, 1948) as developed by van Niel and others (see Lanham, 1952; Madison, 1953).

Certain of the concepts of protein synthesis presented by Haurowitz (1950) deserve consideration here, since they relate to mechanisms for exact reduplication. These may be summarized as follows: (1) Protein expanded to form a monolayer may serve as a template for autoduplication. (2) Specific adsorption of amino

acids to identical amino acids on the expanded protein layer occurs. (3) Through the action of "nonspecific" enzymes on the adsorbed amino acids an expanded protein film is formed which is a duplicate of the original protein template. (4) Folding of the two-dimensional protein film occurs so that a three-dimensional globular protein molecule is formed. The shape of this three-dimensional molecule will depend on the shape and electrostatic field of polar groups of adjacent cellular structures. These ideas may be adapted to the reduplicating-molecule concept by assuming that a wide variety of substances in addition to nucleic acids, such as phosphate gels, clay, and oil droplets, could serve to adsorb and unroll the simple original proteins. The duplication of these would then be presumed to occur as a result of the adsorption of energy-rich amino acid derivatives rather than amino acids, since no "nonspecific" enzymes required in the Haurowitz model would have been available to link amino acids.

The original "protocells" envisioned by Oparin (1938) consisted not of single molecules or of associations of small numbers of molecules, but rather were coacervate droplets. These were condensed from an environment rich in colloidal material. Concerning division, Oparin suggested that the postulated coacervate droplet continued to grow by adsorbing or condensing additional material until it was fragmented by external mechanical forces or by surface tension. He further pointed out that droplets whose properties favor fragmentation would tend to maintain a more favorable relation between surface area and mass, and would thereby increase the adsorption of dissolved substances. Thus a coacervate droplet endowed with the ability to divide was said to have a definite advantage over other droplets.

The attempt by Oparin to apply the concepts of coacervation to the origin of life is open to several criticisms. These apply equally well to several other attempts to use the term in connection with subcellular particles where authors have been more concerned with the morphology of coacervates than with the colloid chemistry involved. A coacervate is considered to be a colloid-rich system in equilibrium with a colloid-poor solution (the equilibrium liquid) (Bungenberg de Jong, 1949a). In contrast to the reduplicating-molecule theory, where one must account for the appearance of one or two special colloidal molecules, the coacervate theory requires a whole sea-full of them. Although it is true that these are not considered to be self-duplicating at the outset, the difficulties in accounting for the production of protein molecules on this scale are insurmountable. To postulate that the coacervation occurred in a small lake or pond does not help greatly, since ultraviolet degradation or a lack of sufficient substrate molecules would soon bring the venture to an end. Since a coacervate is a colloid-rich phase which can be formed only in equilibrium with a more dilute solution of the same colloids, it is evident that all coacervate droplets in the same system will tend to be similar in composition and structure even though very complex. When the droplets begin to differ one from the other, they are no longer simple coacervates. This is true whether the differentiation consists of a smaller average size giving a droplet a higher growth rate, as mentioned by Oparin, or if autocatalysis appears. In the latter instance, new autocatalytic molecules would tend to be lost from the droplet unless certain additional changes such as the appearance of a semipermeable membrane are postulated. Either the coacervate theory should be altered to conform with what is known about coacervates, or the systems postulated by Oparin should be described in other terms.

In the theory of the reduplicating or autocatalytic molecule, it has been proposed that a vast supply of organic compounds present in the environment were used for reduplication and that no special enzymatic activities were present. In the simplest case, division is presumably taken care of by random breakage of long, growing chains.

It appears more likely that the first stages in the transition to what might be called life involved single autocatalytic molecules. These may well have been relatively small compared with present-day protein, nucleic acid, or nucleoprotein molecules. If condensed from relatively energy-rich intermediates, their initial formation would present no insurmountable obstacles. When the quantity of reactants is measured in terms of kilotons, the formation of almost any type of molecule becomes a likely event even if the equilibrium constants suggest otherwise to the chemist accustomed to considering gram quantities.

The difficulty at this point is that there is little experimental knowledge of organic autocatalytic molecules. The first reasonable model of a self-duplicating (autocatalytic) system which

may possibly be capable of other activities (heterocatalysis) is that proposed for deoxyribonucleic acid (DNA) by Watson and Crick (1953; Gamow, 1954). The interesting concept that nucleotides and amino acids are the only building blocks suitable for constructing a complex living system has recently been suggested by Bragg (1954). Certainly the primeval environment provided sufficient time and materials for a thorough experimental investigation of a variety of possibilities.

In the laboratory, autocatalysis by large molecules has not been demonstrated in the absence of life. In a cell, autocatalytic molecules exist in a very special environment which stands little chance of being duplicated outside the cell at present. The possibility exists that autocatalytic molecules have been isolated but that suitable conditions for demonstrating autocatalysis have not been worked out. The temptation is to expect such molecules to reduplicate rapidly. However, under the conditions which may be devised, or in the primeval "soup," autocatalysis may proceed at a very slow rate. Thus a molecule which required one or several years for reduplication could easily be a "life ancestor" but be overlooked in the laboratory. The mechanisms by which the daughter molecules of an autocatalytic duplication could be made to separate will be considered in a subsequent section on chromosomal condensation.

With the formation of specific enzymes necessary to synthesize certain substrates whose concentration in the environmental "soup" has been depleted by "vital" activity (Horowitz, 1945), the protocell becomes more complex. Since it is assumed that these newly developed enzymes remain associated with the original self-duplicating molecule, and in the first instance are probably produced by it, a point of complexity may soon be reached where reduplication of the original molecule and associated protein and its separation into two can no longer be presumed to involve a separation of a variety of associated enzyme molecules (primordial cytoplasm). It is at this stage of development that the origin of some mechanism for separating a constellation of associated colloidal particles into two similar associations must be postulated. In some respects the reduplicating molecule developed to this stage of complexity resembles the coacervate droplet postulated by Oparin. This is also true of systems such as those condensed on oil films (Haldane, 1933) or clay particles (Bernal, 1951) at a later stage in their development. It becomes necessary, therefore, to consider the origin and development of a mechanism for cell division.

Oparin (1938) suggests that mechanical forces, including the actions of waves and currents, account for early divisions. This may have sufficed under certain local conditions in systems containing large numbers of similar molecules. Here no even distribution of reduplicating material is necessary, since all daughter "cells" would contain representatives of all molecular species (primitive endopolyploidy). It does not appear reasonable to assume that this dependence on external forces for division persisted for long. On the other hand, it does not appear justifiable to postulate the sudden appearance of a special mechanism devoted solely to cell division. On the contrary, it appears necessary to propose the nonexistence of any new specific differentiated mechanism to account for division in a protocell and to look for properties which are inherent in such entities and which will result in division automatically.

At this level of complexity many of the theoretical treatments of Rashevsky (1941a, b, 1948, 1952) and Landahl (1942a, b, c, 1943) are pertinent. Certain of these approaches have been recently reevaluated by Rashevsky (1952). The diffusion drag-force theory (Rashevsky, 1938, 1939; Landahl, 1942a), which will probably find an important application in explaining the movements of such actively metabolizing centers as the mitochondria and possibly the centrospheres, does not appear to be applicable to very simple systems with very low metabolic activities. Additional difficulties with this theory have also been presented (Rashevsky, 1952).

Elastic stresses in gels have also been considered by Rashevsky (1948) as possible causes of cell elongation and division. It was concluded from considerations of the theory of plasticity, through the application of Betti's theorem, that elastic forces produced by gelation could not cause division. However, this conclusion has now been shown to hold only in the case of a homogeneous system (Isenberg, 1953). Since living systems generally contain both micro and macro viscosity gradients (Seifriz, 1952), it has been possible to develop a mathematical theory of cell division based on elastic stresses in colloidal systems (Rashevsky, 1952). If we assume the applicability of the theoretical treatments re-

ferred to, it then becomes necessary to consider at some length the nature of biochemical events which alter viscosity and cause sol-gel changes in living systems.

Fundamentally, gelation involves cross linking between adjacent macromolecules to give a semisolid structure exhibiting a yield value (Hermans, 1949).

[A yield value is a property characteristic of the solid state. A solution exhibiting it will resist flow up to a given shearing force. It behaves as an elastic solid below that tension.]

The folding and unfolding of protein chains, so frequently invoked to account for biological phenomena (Frey-Wyssling, 1949; Loewy, 1949; Goldacre and Lorch, 1950; Meyer and Mark, 1951; Goldacre, 1952), is relevant here only to the extent that such folding and unfolding alters the number and availability of cross-linkage sites. Thus the changes occurring when fibrinogen is changed to fibrin would result in only a small viscosity increase in the blood if the only change were an unfolding. As is well known, the extensive cross-linking accounts for the gelation or clotting observed. Although changes in consistency which may be termed gelation are seen in both normal and pathological cells, little is known directly of their true nature. It has often been likened to the clotting of vertebrate blood (Heilbrunn, 1928, 1952; Lettré, 1952). This analogy may have been useful in the past, but its value is questioned here for several reasons.

(1) The blood-clotting mechanism, though far from completely understood, has nevertheless been made to proceed in systems composed of relatively pure substances whose properties are fairly well defined. No similar successful isolation of the *components* of a cytoplasmic "clotting" mechanism has been described. Experiments relating to this point will be presented in a subsequent paper. (2) The thromboplastic substances present in the cell do not appear to be present in an inactive state, as would be expected if they were part of a cell-clotting mechanism. (3) Sol-gel changes in the normal cell are readily and rapidly reversible (Chambers, 1917, 1921; M. R. Lewis, 1923, 1934; Marsland, 1951). This is not the case with the clotting of blood. (4) Changes in *p*H which do not dissolve blood clots can cause wide variations in cytoplasmic viscosity. (5) On purely theoretical grounds, if an analogy is valid, a two-directional flow of information and ideas might be expected. Thus, if blood coagulation resembles the cytoplasmic viscosity changes occurring during cell division and if research on blood coagulation furnishes clues useful in the study of cell division, as has been the case with the effects of certain anticoagulants, then it should be expected that studies on cell division would also suggest ideas and effects which would increase the understanding of blood clotting. This does not appear to have been the case. Furthermore, the analogy creating the impression that more is known than actually is about cytoplasmic behavior, tends to channel thinking and experimentation, and obscures many observations inconsistent with the concept. Although certain details of the two systems may ultimately be found to be similar, the comparison does not appear to be a fruitful one and, for the purposes of this discussion, will be discarded.

With regard to the folding and unfolding of protein chains, it should be noted that such changes are generally studied at air-water interfaces, which obviously do not exist within the cell. The surfaces which may exist within cells which contain few fat droplets probably involve very small surface tension forces. It is evident also that it is not possible for more than a small fraction of the protein molecule population of a cell to be at interfaces at any one time. In a clear, granule-free cytoplasm such as is seen in centrifuged cells, there seems to be no obvious mechanism for the denaturation, unfolding, or the refolding of proteins. Yet fairly large changes in viscosity are thought to occur. The local nature and non-Newtonian character of many of these alterations has been justifiably emphasized (Seifriz, 1952). No adequate treatment of the energy requirements for chain folding and unfolding has been presented (Seifriz, 1953).

It is suggested that the sol-gel transformations in the cytoplasm may be best described in terms of reversible cross-linking, not of unrolled polypeptide chains but of beaded chains formed by the linking of *intact, undenatured* macromolecules. The junction-point energies involved are in general rather similar and low as occurs in the so-called type III gels of Freundlich (1937; Marsland, 1951). These show a slight increase in volume on gelation.

In any colloidal system, particles with opposite charges will tend to flocculate out. It would appear, then, that the colloidal stability of a cell depends on maintaining a state of affairs such

that the vast majority of particles, in the cytoplasm at least, have a *like* charge. The question of the sign of the charge on cytoplasmic particles is therefore an important one, and one which has been the subject of considerable controversy. For the purposes of this discussion the predominant charge on cytoplasmic colloids generally is assumed to be *negative*. The reasons for this conclusion are many and will be discussed in a subsequent section. They may be summarized here as follows: (1) The nucleic acids, most tissue proteins, and the colloidal constituents of protoplasm generally have an *acid* isoelectric point; (2) the cations of the cell are largely monovalent; (3) the cytoplasm and cytoplasmic constituents, both inside (microinjection) and outside (surface precipitation, brei studies) the cell are flocculated or precipitated by multivalent cations; (4) electrophoretically, cytoplasmic constituents pile up at the anode; (5) tissue breis take up added calcium (Weimar, 1953) and flocculate (Gross, 1952); and (6) fresh cytoplasm and cells fixed without removal of nucleic acids are generally basophilic (exceptions will be noted later).

In a colloidal system of negatively charged particles, the simplest approach to viscosity or sol-gel changes is to consider the types of low-energy (reversible) cross-linkages which may occur between macromolecular polyanions to form beaded chains. In a fairly concentrated system such as the cell cytoplasm, changes which could be observed as flocculations when in dilute solutions may appear as gelations or as increases in viscosity. Thus lowering the cell pH produces an increase in viscosity or consistency (Loeb and Blanchard, 1922; M. R. Lewis, 1923; Barth, 1929; Minshall and Scarth, 1952), whereas in more dilute systems such as tissue homogenates, lowering the pH will result in flocculation (Dounce, 1950; Anderson, 1950). Similarly, cations with more than one charge have a pronounced effect on such systems. The addition of calcium in low concentrations will precipitate nucleoproteins (Taylor, Greenstein, and Hollaender, 1948) and will shrink isolated nuclei (Wilbur, Anderson, and Skeen, 1949; Wilbur and Anderson, 1951; Schneider and Petermann, 1950; Anderson and Wilbur, 1952). If more calcium is added, the familiar reversal of charge occurs, the nucleoproteins go back into solution, and isolated nuclei swell. With cations of increasingly higher valence, a very strong precipitating effect is seen, but there is much less tendency toward re-solution in the presence of excess cation (Bungenberg de Jong, 1949b).

These concepts may be applied to living systems generally by considering the degree of polymerization of positively and negatively charged groups in the cell. Since it is obvious that electrical neutrality must exist, there must be an equal number of cationic and anionic groups or charges. However, insofar as gross changes in colloidal stability are concerned, the effect of divalent and multivalent electrolytes so far outweighs the effects of monovalent ions that the effects of the latter may be neglected. A typical cell therefore consists of a series of highly polymerized negative charges (nucleic acids, sulfated polysaccharides, and proteins with an acid isoelectric point) with only a few polycations of varying sizes (histones, protamines, cytochrome c, the basic polypeptide described by Bloom and Blake (1948), spermine, spermidine, agmatine, and other multiply-charged amines). The greater part of the positive charge resides in potassium, with smaller additional amounts in Na^+, Ca^{++}, and Mg^{++} and in the amino groups of otherwise negatively charged proteins. The calcium and magnesium would be expected to be bound to the polyanions present, and this indeed appears to be the case experimentally (Weimar, 1953; Gross, 1952). A small shift in the degree of polymerization of the positive charges will have a profound effect on such a system. This has been demonstrated repeatedly in a wide variety of colloidal solutions. In these considerations the important things are the degree of polymerization of the charges, and their quantitative ratio. These two factors characterize the *balance of polyelectrolytes* in the cell. Experimentally, the polyelectrolyte balance in cells may be altered by injecting polyanions (heparin, sulfated polysaccharides, nucleic acids, and polyacid dyes) with a resulting solation; or by injecting polycations (heavy metals, protamine, and basic dyes) with a resulting gelation. The factors which are thought to cause a shift in polyelectrolyte balance are listed in Table 1.

Cell colloids, with the exception of substances such as dextran or glycogen, may be classified as polycations, polyanions, or polyampholytes. The majority of proteins would probably be included in the last group. In this discussion the term polyampholyte has not been used because it has been considered necessary to stress the slight excess negative charge of most polyampholytes in the cell. It is preferred here to refer to poly-

TABLE 1

Factors causing a shift in the balance of colloid-associated charges

Shift toward polyanions (Solation)	Shift toward polycations (Gelation)
Synthesis of polyanions	Synthesis of polycations
Addition of polyvalent anions	Addition of polyvalent cations
Rise in *p*H	Drop in *p*H
Depolymerization of polycations	Depolymerization of polyanions

ampholytes as either weak polyanions or weak polycations. Instances where the charge distribution over the surface of a colloid is such that it becomes a giant dipole are discussed in a subsequent section on fibril formation.

It has been tacitly assumed that the basis for movement in all cells is ultimately to be found in macromolecular structure of some type. The necessity for such an assumption has been presented by Frey-Wyssling (1953). The changes in viscosity or consistency which occur generally involve little or no change in the concentration of dissolved substances in the cell. The physical alterations observed must therefore involve changes in either the physical state of the macromolecules present, or in their associations.

The unrolling of either globular proteins to form long polypeptide chains, or of rolls of preformed chains of proteins (Kopac, 1951) is considered unlikely. It appears simpler to consider that the submicroscopic structures which are constantly being formed and broken down in the living, moving cytoplasm are formed by the association of cytoplasmic protein molecules *without* either unrolling or denaturation. The resulting chains are beaded and of varying length and with varying degrees of cross-linking between chains. No special proteins need be postulated for this purpose since, as will be shown in a subsequent section of fibrillization, such chains may be formed experimentally from a variety of ordinary proteins. The bonds which hold macromolecules together have been discussed in some detail by Frey-Wyssling (1953) and are the following: (1) a homopolar cohesive bond, which accounts for the mutual attraction of lipidic groups; (2) a heteropolar cohesive bond, which occurs between groups of pronounced dipole character (hydrogen bonds); (3) heteropolar valency bonds, which occur in salt formation; and (4) homopolar valency bonds, such as occur in disulfide linkages.

Frey-Wyssling has pointed out the difficulties involved in attempting to determine experimentally which type of bond is important in any one system. A procedure which is designed to alter one type of linkage in the cell may in fact alter several.

In a living system the important thing is not how many different types of bonds may bind macromolecules together, but rather, which one or ones can be *varied* either in number or strength, and can be *easily broken and reformed*. The temperature dependence of cytoplasmic viscosity between 10° and 18°C. in the amoeba may indicate that homopolar cohesive bonds are involved, as Frey-Wyssling has suggested. However, the problem in cell division is how to explain changes occurring at *one* temperature in a system involving no wide fluctuations in *p*H, redox potential, salt concentration, or pressure. No obvious mechanism for reversibly masking or altering homopolar or heteropolar cohesive bonds between proteins has been postulated. The homopolar valency bonds, such as occur in the disulfide linkages in wool or keratin, are generally ruptured only by relatively drastic means.

[Evidence suggesting that R—SH HS—R $\rightleftarrows$ R—S—S—R bonds may be implicated in certain aspects of mitosis in contemporary cells will be discussed in a subsequent paper.]

The heteropolar valency bonds (salt linkages) remain. These are the bonds which link polyelectrolytes containing areas or groups with opposite charges.

Thus, although several types of bonds may participate in the formation of structure by linking macromolecules together, the salt linkages are believed to be the ones chiefly responsible for the continuously variable affinities of macromolecules in the cytoplasm.

A shift in the balance of polyelectrolyte charges in favor of polycations in a predominantly polyanionic cytoplasm will favor the formation of a large number of salt linkages between the constituent macromolecules. The result is, first, bonding to form dimers and trimers, and then the formation of longer beaded chains with variable degrees of cross-linking. A further shift will lead to contraction of the chain. A shift in the direction of polyanions will return the system to a state of discrete molecules in solution. The concept of

polyelectrolyte balance has been used here as a unifying principle to relate all the various effects listed in Table 1. In the cytoplasm of the nondividing cell the local shifts in polyelectrolyte balance which account for the movements observed (other than those caused by diffusion gradients) are most likely related to changes in the degree of polymerization of phosphoric acid groups associated with adenylic acid, i.e., the synthesis and breakdown of the polyanion, adenosine triphosphate (ATP).

The proposed primeval mechanism consists therefore of a cyclical variation in the relative proportions of polycationic and polyanionic charges occurring during the growth of a protocell. In the growth period (interphase) the cell volume increases and is composed of predominantly polyanionic colloids. At the end of this phase an increase in the number of polymerized cationic groups relative to the number of polymerized polyanionic groups occurs. This is not thought to be necessarily due to the production of any new and different substances, but rather to a change in the *relative rates* of synthesis of two substances normally being produced.

During the course of cellular evolution this mechanism has doubtless undergone numerous alterations and refinements. For example, shifts in the balance of polyelectrolytes may well occur as a result of a small change on the surface of a colloid rather than as a result of synthesis of new ones.

Taking into account the predominant negative charge on cell colloids and the effects of shifts in polyelectrolyte balance on the state of the colloids, one may construct the following picture of the origin of the dividing mechanism. The majority of the complex building blocks necessary for reduplication of the original pseudocoacervate or nucleoprotein-enzyme associates (protocells) are thought to have occurred in the primeval seas (Haldane, 1933; Oparin, 1938; Alexander, 1948; Horowitz, 1945; Blum, 1951; Urey, 1952). As the size of such protocells increased, the rate of synthesis of any particular compound (nucleic acid or protein) would depend on the substrate concentration and the rate of diffusion of the substrate molecule to the site of utilization. For any short period of geologic time the environmental concentration is assumed to have remained constant. Differences in the diffusion rates of nucleotides and amino acids could be expected to favor the synthesis of proteins over nucleic acids in larger cells, since amino acids are generally smaller than nucleotides. Also the concentration of the amino acids was probably higher than that of the nucleotides, since the latter are more complex molecules and would probably not be synthesized at as high a rate. The proteins generally found associated with DNA are rich in diamino acids. If the synthesis of such proteins continues while the production of nucleic acid diminishes, the net effect would be a shift in the balance of polyelectrolytes, resulting in local areas of gelation and contraction throughout the cell. The effect would be to produce a stressed gel system with local variations in viscosity such as has been treated mathematically by Isenberg (1953) and by Rashevsky (1952), and consequently resulting in *cell division*.

THE INITIATION OF CELL DIVISION

The initiation of cell division will be considered in terms of a shift in the balance of polyanions and polycations.

Various substances and treatments have been shown to stimulate or to delay the division of cells (E. N. Harvey, 1910; Loeb, 1913; Lillie, 1926, 1931, 1941; Morgan, 1927; E. B. Harvey, 1940; Tyler, 1941; Marshak and Walker, 1945; Wilson and Leduc, 1947, 1950; Harding, 1951; Shaver, 1953). Danielli (1951) has classified a number of these as acting either on the surface or on the interior of cells. However, it has not been possible to relate all the active agents to one simple biochemical event or chain of events in the cell directly or indirectly. Heilbrunn (1952) has considered that the common denominator is the stimulation of the cell which involves the release of calcium. Danielli, however, has preferred to believe that the release of calcium is a secondary event. Until the biochemistry and physical chemistry of stimulation is better understood, these differing points of view cannot be fully evaluated. In this discussion the effects of several stimulants of cell division will be interpreted in the light of their effects on the balance of polyelectrolytes within the cell.

In the egg cell the most obvious agent for inducing cleavage is the sperm, which characteristically contains an abundance of very basic protein (polycation). Thus, if it is assumed that the genetic pattern or code is carried on the DNA, the stimulus for cell division could reside in these basic proteins which, in the case of many fishes (Miescher, 1897; Kossel, 1928) and of the chicken (Daly, Mirsky, and Ris, 1951), have been shown to consist almost entirely of the extremely simple

subprotein, protamine. This substance may contain over 85 per cent of one diamino acid, arginine (Hamer and Woodhouse, 1949). The chemistry of nucleoprotamines and protamines has been intensively reinvestigated by Felix and coworkers (1951, 1953).

Several observations suggest a causal relation between basic proteins and the initiation of cell division. According to Bataillon (1929), the amphiaster in the anuran egg activated by the puncture method is derived from a cytaster which arises only when the puncture introduces some foreign *nuclear* material in the form of leukocytes or other cells which occur in the egg jelly. It has been shown that isolated nuclei from brook trout sperm (*Salmo fontinales*) can be used to activate eggs (Felix, Hartleib, and Krekels, 1952). The nuclei contained little besides basic protein and DNA. Karyometric studies suggested that the embryos were haploid, however, and that the chromatin material from the isolated nuclei probably was not used (Schneider, 1953). Protamine ". . . is one of the most efficient substances for the causation of artificial parthenogenesis" (Loeb, 1913). Since many eggs possess jelly coats which precipitate with protamines, these substances have received little attention. It appears quite possible that a number of other polycations may have similar effects, since such unphysiologic substances as methylene blue are parthenogenetic. The basic polypeptide described by Bloom and Blake (1948) deserves attention in this respect since it appears to be a normal tissue constituent. Shaver (1953) found cleavage-initiating substances in microsomes, but noted that this negative results with nuclear material were probably due to the injection of too large an amount rather than to the absence of activating substances from the nucleus.

If polycations are causally related to cell division, as here proposed, then polyanions should inhibit the initiation of cell division. In fact, if the experiments had not already been done, they would be listed as being crucial to the present approach. The inhibition of cell division by acid polysaccharides such as heparin has been demonstrated by a number of authors (Goerner, 1930; Zakrzewski, 1932; Fischer, 1936; Balazs and Holmgren, 1949; Heilbrunn and Wilson, 1949, 1950; Harding, 1949; Heilbrunn, Wilson, and Harding, 1951; Chaet, 1952) and is probably a very general phenomenon. The simplest explanation is that, as a large and strongly charged polyanion, heparin shifts the polyelectrolyte balance of the cell by combining with any basic substances present (Anderson and Wilbur, 1950, 1951; Roberts and Anderson, 1951). It would be of interest to know whether the cyclic polyphosphates, which are not broken down in the rat (Gosselin et al., 1952), also inhibit cell division.

In regard to the effects of ATP on cell division, it is difficult to distinguish between the effects of this substance as a polyanion and as a source of energy for the synthesis of numerous other substances. Thus, if ATP furnished the energy required to synthesize basic proteins, the net effect of adding it might be different from that predicted purely on the basis of the number and strength of its charges. Certainly the effects of ATP inside and outside the cells appear to be drastically different (Green and Stoner, 1950). Bullough (1952) has reviewed the data on the role of ATP as an energy source in mitosis.

Harding (1951) has summarized the evidence for the initiation of cell division by a number of *acid* substances obtained from damaged cells. Experiments both cited and presented by her indicate that the active principles were generally among the lower fatty acids and that the effect was observed *only at an acid* pH. The parthenogenetic effect of acids is well known (E. N. Harvey, 1910; Chambers, 1921; Lillie, 1926, 1941; Tyler, 1941). As was noted in the previous section, polyelectrolyte balance may be shifted effectively in favor of polycations by lowering the pH. The effects of acids added to a cell suspension on the pH of the cell interior would appear to depend on the permeability of the cell to the anion in question. As has been known since the early work of Overton, lipid-soluble substances generally penetrate cells more readily than substances which are not lipid-soluble. The lower fatty acids, by virtue of their negative charge and their nonpolar groups—which enable them to penetrate cells—may be expected to influence intracellular pH rather readily and to have a basic protein-mimicking or "sparing" effect in egg cells. The activating effect of heat may find a similar explanation, since it has been interpreted as being due to increased acid formation in the egg (Lillie, 1931).

Considerable emphasis has been placed on the role of calcium in the physiology of the cell (Heilbrunn, 1952). Danielli (1951) has questioned whether this element is involved in the primary phases of cell stimulation and has suggested instead that calcium can be released only by (1) the production of another cation which is preferentially bound in its place, (2) the production of

acid (or some equivalent process) which will reduce the number of ionizing acidic groups of the surfaces of the cell colloids, or (3) the conversion of these colloids into units of smaller molecular weight, for example, the conversion of a protein into amino acids. Thus it would appear that calcium may serve as an *indicator* of shifts in polyelectrolyte balance within the cell, by virtue of its release under conditions which favor an increase in effective polycation concentration. A detailed reinterpretation of much of the experimental data used in support of the central role of calcium in cell stimulation appears feasible but will not be attempted here.

The role of the calcium ion in the initiation of cell division has been stressed by Dalcq, Pasteels, and Heilbrunn (see review by Tyler, 1941). In a wide variety of cells calcium has been shown to be capable of producing activation and to be necessary for the full effectiveness of a number of parthenogenetic agents. From the point of view of the theory presented here, calcium may be expected to assist in the displacement of polycations in the cytoplasm and, like acid, to have a polycation-"sparing" action. In a loaded system, such as a marine egg, it appears that a variety of colloidal substances must be held in readiness in a functionally inactive condition awaiting fertilization. The polycations stressed here, which may well include histones poured into the egg cytoplasm by nurse cells, must be bound or restrained. Calcium or any other salts in concentrations above that normally found in the cytoplasm may be expected to release part of the bound histone or other basic substance much as histone is released from DNA by strong saline. When the egg is returned to sea water, the basic substances are again bound, but at *different sites*. Thus if AB represents the original inactive bound condition (B = basic substance, A = binding site), and BC represents the active condition where C may be a fibril-forming protein or may be DNA ready to be condensed, then the reaction

$$AB + C \xrightarrow[\text{Ca}^{++} \text{ or KCl}]{} A + B + C \xrightarrow[\text{sea water}]{} A + BC$$

would lead to the formation of structures characteristic of the BC complex (spindle fibers, condensed chromosomes, etc.). The well-known activation of marine eggs by hypertonic solutions (Loeb, 1913; Morgan, 1927; Tyler, 1941) is thus readily harmonized with the views presented here.

As to the stimulus to cell division in contemporary cells, it is probable that the production of the basic substances stressed here is a highly specialized and well-controlled process, in contrast to the condition postulated for primeval cells where differences in diffusion rates and concentrations of nucleotides and amino acids were effective.

The stimulus to cell division observed after injury to part of a tissue or organ may well be due to the acid "injury substances" studied by Harding (1951). However, a number of aspects of autolysis should not be neglected. The production of amines under such conditions is well known (e.g., cadaverine, putrescine). The possible stimulating effects of such substances remains to be investigated. Little is known concerning nuclear constituents after cell death. The breakdown of nucleic acids by intracellular nucleases (Oes, 1908, 1910 cited by Hughes, 1952) and of protamines by cathepsins (Maver and Greco, 1949a, b; 1950) has been adequately demonstrated. However, the relative rates at which these processes might occur in autolysing cells is not known. The possibility that the nucleic acids may break down sufficiently to release the basic proteins after tissue damage deserves consideration. It should be noted that the injection of isolated liver chromatin material into rabbits apparently increases the mitotic rate in the liver (Marshak and Walker, 1945).

Recent work on the rate of turnover of DNA during cell division suggests that this rate may be twice as high as would be expected from the number of cells produced (Barnum, Huseby, and Vermund, 1953; Stevens, Daoust, and Leblond, 1953; Daoust, Bertalanffy, and Leblond, 1954). Although this work has been questioned (Barton, 1954), it appears possible that twice the amount of nucleoprotein necessary for the normal complement of the two daughter cells is produced, but that half the DNA produced is broken down. This could occur in such a manner that there would be only small changes in the total amount present in the nucleus at any one time. The net result would then appear to be a doubling of the DNA and a quadrupling of the histone.

Bloch and Godman (1955), however, conclude that DNA and histone synthesis proceed simultaneously and that they are present in constant proportions. Nevertheless, the standard error for their histone values was very large; and no source of the variability could be adduced. The possibility exists, therefore, that a small excess of histone may be produced in the nucleus before cell division.

Since histone turns over much more rapidly than DNA (Brunish and Luck, 1952), it is evident that it is either broken down in situ, or that it escapes the nucleus and perhaps serves some other function in the cytoplasm. The rate of histone synthesis may well change markedly during the various stages of cell division, and the amount present could vary considerably without being at variance with the available data. Such variation could effectively shift the balance of polyelectrolytes in the cell and thereby control cell division.

It was considered of interest to postulate, on the basis of the theory presented here, a substance which might fulfill the requirements of a simple physiological polycation and to investigate its effects on dividing cells. Decarboxylated arginine (agmatine) was chosen for trial since it could be readily produced from arginine, and because it possesses a double negative charge. Experiments were performed (St. Amand, Anderson, and Gaulden, 1955) with grasshopper neuroblasts by using the technique and culture medium described by Carlson, Hollaender, and Gaulden (1947). In these cells the duration of several stages of cell division may be accurately timed. In a series of four experiments, 0.005 *M* agmatine shortened the time from the beginning of prometaphase to the end of metaphase by 32 per cent, did not alter the length of anaphase, but shortened early and middle telophase by 37 per cent and 6.3 per cent, respectively. Further observations on six different preparations similarly treated showed that agmatine increased the number of cells going through cell division in *each* preparation, with an average increase of 80.6 per cent over a three-hour period. The increased number of cell divisions is sustained for at least five hours. *Thus, it appears that agmatine enhances the rate of changes normally occurring in all mitotic stages except anaphase.*

Substances which accelerate mitosis are rare. It is rather unusual, therefore, to select with no prior experimental knowledge a single substance which does this effectively. These results constitute the most satisfactory experimental results stimulated by this theory to date.

The recent isolation and synthesis of kinetin (Miller et al., 1955a and b), a factor which stimulates cell division in plants, adds further support to the concept that basic substances are causally related to the initiation of cell division. This substance, which is active in concentrations as low as 0.01 p.p.m., appears to be 6-furfuryl-aminopurine, a weakly basic derivative of adenine.

Histone and protamine have been frequently mentioned in this discussion because they are the only polycations generally available in any quantity in cells. However, another source of polycationic material deserves investigation. In the most general case, cell division may be considered as resulting from an imbalance between the non-growing nucleus and the growing cytoplasm. If a substance *X* is produced in proportion to the mass of the cytoplasm, but is utilized in proportion to the mass of the nucleus, then it will vary rhythmically in quantity, reaching a peak before each cell division. Quantitatively, the most important cell product is protein. If protein synthesis proceeds by two steps, the first of which is under general cytoplasmic control, with the second under nuclear control, then the products of the first step would tend to accumulate if the cytoplasmic mass were disproportionately larger than the nuclear mass. The detailed steps of protein synthesis are unknown. However, it can be said that polypeptide intermediates *must* exist if for no other reason than that it is inconceivable that a row of amino acids could all be interlinked at precisely the same fraction of a microsecond. Polypeptide intermediates would doubtless include predominantly basic and predominantly acidic molecules. The former would fill admirably the requirements for a polycationic material appearing in excess when the cell has exceeded a certain size. While protein intermediates of this nature have not been found previously, it is suggested that more refined methods will show they exist.

CHROMOSOMAL CONDENSATION

Both the division of the primeval protocells and the initiation of cell division in contemporary cells have been postulated here to be due to a shift in polyelectrolyte balance such as would occur with an increased production of polycations. In this section it will be shown that the same mechanism can serve to account for the condensation of chromosomes into compact bodies such as are observed during metaphase. This mechanism will be treated first as acting on a DNA-protein gelwork and secondly as it may affect the structure of the chromosome as it is thought to exist.

Chromosomal condensation and the control of nuclear volume are viewed as two aspects of the same problem. Here the concept that somatic nuclei generally consist almost entirely of swollen, hydrated, or "extended" chromosomes is followed. Whereas several earlier authors have presented

evidence that the chromosomes swell, forming vesicles which fill the interphase nucleus (Richards, 1917; Kater, 1927, 1928; Lewis, 1947), Ris and Mirsky (1949b) have shown that the swelling is due to a change in the physical state of the DNA and that the chromosomes of the resting nucleus are not merely swollen vesicles. Later work on the enzymatic dissection of the isolated rat liver nucleus gives little evidence of internal nuclear septation or vesicular structure (Anderson, 1953b) and supports the view of Ris and Mirsky. The volume of the interphase nucleus (minus the nucleolar volume) and the combined volumes of the metaphase chromosomes indicate the limits of the swelling and shrinking of the chromosomal material which may occur normally. At the outset, therefore, it is instructive to consider the factors which influence the size of nuclei and may alter their volumes, since the same factors may be important in chromosomal condensation.

Numerous studies have been concerned with the effects of various solutions on nuclei. These include the effects of salts on nuclear structure (Strugger, 1930; Shinke, 1937; Zollinger, 1948; Chambers and Black, 1941; Bank, 1941; Duryee, 1937; Laskowski and Ryerson, 1943; Ris and Mirsky, 1949b; Kassel and Kopac, 1950), changes in structure produced by acids and alkalis (Zollinger, 1948; van Herwerden, 1924; Zeiger, 1935; Dangeard, 1947), and in volume changes accompanying changes in tonicity (Churney, 1941, 1942; Callan, 1949; Goldstein and Harding, 1950; Shinke, 1937; Beck and Shapiro, 1936; Shapiro and Parpart, 1937) which were interpreted as evidence that the nucleus behaved osmotically. These studies raise the possibility that chromatin condensation may be due to changes in salts, *p*H, or tonicity. Sufficiently wide variations in the intracellular concentrations of simple salts or in *p*H to account for the condensation of chromosomes, however, do not appear to occur. But if the nuclei behave osmotically, at least the possibility exists that volume changes observed in chromatin during cell division reflect changes in the concentration of solutes within the cell. This problem has been examined in some detail on isolated nuclei, and it has been found that such volume changes are due, at least in somatic cells, to certain colloidal properties of the nuclear substance (Anderson and Wilbur, 1952) and do not indicate that the nuclear envelope is a semipermeable structure. Although results obtained with isolated cell components must be interpreted with caution—a point the

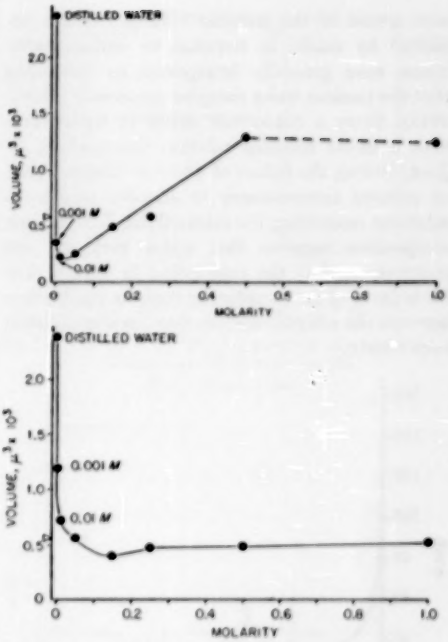

FIG. 1. EFFECT OF VARIOUS CONCENTRATIONS OF $CaCl_2$ (TOP), AND NaCl (BOTTOM) ON THE VOLUMES OF ISOLATED RAT LIVER NUCLEI
(From Anderson and Wilbur, 1952).

author has repeatedly made—*no* evidence is available which indicates that the nucleus of the intact somatic cell differs in its permeability from the isolated nucleus (Anderson, 1953a). A summary of the effects of various solutions on isolated rat liver nuclei adapted from a previous study (Anderson and Wilbur, 1952) is given in Fig. 1. Marked volume changes in response to different salt concentrations are observed, but the nonosmotic character of these changes is apparent from an examination of the curve for calcium chloride. Here maximal shrinkage is obtained with a concentration slightly higher than 0.01 *M* calcium chloride. Swelling is observed at both *higher* and *lower* concentrations. These findings are explicable in terms of a gel-like material composed of strands bearing a negative charge. The major functional component of these strands is believed to be DNA, since extraction of this substance (Ris and Mirsky, 1949b) or its digestion by deoxyribonuclease (Anderson, 1952, 1953c) abolishes the response to salts.

It should be noted that many earlier workers

were aware of the peculiar volume changes exhibited by nuclei in response to various salts. These were generally interpreted as indicating that the nucleus was a complex coacervate (Bank, 1941). Since a coacervate exists in equilibrium with a dilute colloidal solution (Bungenberg de Jong, 1949a), the failure of whole or broken nuclei or isolated chromosomes to dissolve readily in solutions resembling the intracellular fluid in ionic composition suggests that either they are not coacervates, that the equilibrium is shifted very far in favor of the complex, or that the equilibrium between the complex and the solution is established very slowly.

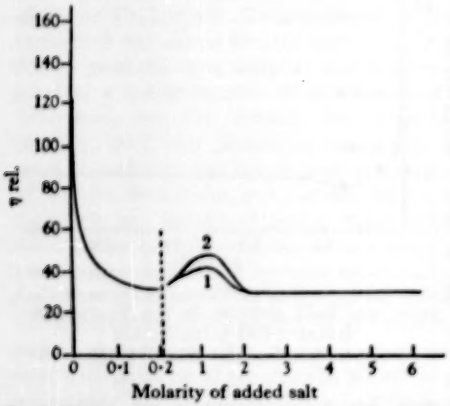

FIG. 2. EFFECT OF SODIUM CHLORIDE ON THE VISCOSITY OF DEOXYRIBONUCLEIC ACID
(From Gulland and Jordan, 1947).

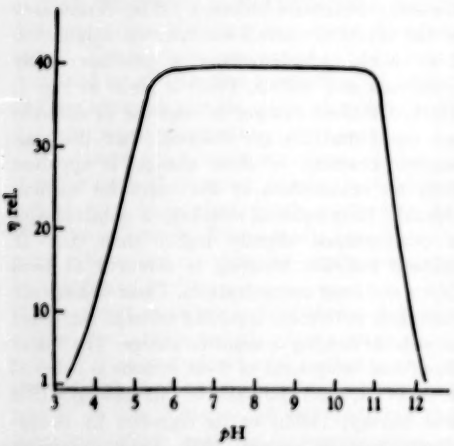

FIG. 3. VISCOSITY OF THYMUS DEOXYPENTOSE NUCLEIC ACID SOLUTIONS AS A FUNCTION OF *p*H
(From Gulland and Jordan, 1947).

The behavior of nuclei and chromosomes, as described above, finds striking parallels in a number of properties which the DNA molecule exhibits in solution. The high non-Newtonian viscosity of DNA is markedly affected by the concentration and type of salts present (Jordan, 1950, 1952; Basu, 1951). In the absence of salts, the ionization of the phosphate groups gives rise to mutually repulsive charges along the chain, and results in a stiffening of the molecule and a high anomalous viscosity (Alexander and Hitch, 1952). With small increments of sodium chloride, a large drop in viscosity is seen (Fig. 2). After a concentration of about 0.15 *M* is reached, little further change in viscosity is observed with added salt. These changes are believed to be due to repression or neutralization of the repulsive forces along the length of the molecule, so as to result in a folding or coiling of the previously extended structure. The sensitive manner in which the shape of ionizable polymeric molecules depends on the degree of ionization has been stressed by Kuhn et al. (1950). *A striking similarity is noted between the volume changes observed in isolated nuclei in sodium chloride solutions and the molecular changes observed in DNA in similar solutions by viscosimetric methods* (cf. Figs. 1 and 2).

The viscosity (and therefore the degree of coiling) of DNA is also affected markedly by the hydrogen ion concentration. Over the range of approximately *p*H 5–10 the viscosity is rather constant (Fig. 3), dropping at higher and lower values. Below *p*H 5 a decline in viscosity is believed to be due to repression of ionization of the phosphoric acid groups, with the result that the molecule collapses. Thymus nucleoprotein in 1 *M* sodium chloride exhibits a similar uniform viscosity over a range of about *p*H 5–9.5, where a sharp rise and fall are observed (Fig. 4). At alkaline *p*H's the DNA is thought to extend and then hydrolyze spontaneously. Isolated nuclei exhibit remarkably similar behavior, having essentially constant volume over the *p*H range 5–9 in the presence of equimolar phosphate buffers (Fig. 5). At higher *p*H values the nuclei swell and go into solution; below *p*H 5 they shrink. A comparison of the physical properties of the nucleus or of chromatin and of DNA in solution indicates that considerable segments of the DNA chains in the nucleus are free to coil and uncoil, exchange ions, and to behave very much as DNA does in solution. It is difficult to escape the conclusion that the colloidal properties of the somatic cell nucleus are very largely

reflections of the physical properties of the DNA molecule, subject to the following qualifications.

Firstly, it is evident that the DNA in a nucleus suspended in a salt solution approximating the intracellular environment is not in a soluble form. Even if the nuclear envelope is ruptured, it does not pass into solution. This has been demonstrated in the many experiments where nucleoprotein threads or isolated chromosomes have been prepared from nuclei by the use of high shearing forces (Mirsky and Ris, 1947a, b). Schneider and Hogeboom (1951) have questioned whether DNA in the nucleus is in a different state than has been supposed, since a large portion of the DNA from nuclei disrupted in sucrose was not easily sedimentable. The suggestion was made that DNA is not associated with structures comparable to chromosomes but is colloidally dispersed within the resting nucleus. Since nuclei and chromosomes swell markedly in ion-free sucrose media, and since in the absence of salts nucleoproteins can be dissolved out of nuclei (Bernstein and Mazia, 1953) and chromosomes, this argument does not appear to hold. Certainly the interphase nucleus does not normally exist in a salt-free environment.

Secondly, although the volume changes exhibited by isolated nuclei (Anderson and Wilbur, 1952), chromosomes, and nucleoproteins (Jeener, 1946) in response to salts indicate that a considerable number of segments of the DNA chains are free to bind various ions and to coil and uncoil, parts of these chains must be concerned with cross-linking or interlinking. The available data suggest that both in the nucleus and in isolated nucleoproteins the cross-linking and restraining is done by basic proteins such as histone or protamine.

The following evidence suggests that the bonds are predominantly of the salt or ionic type. Strong salts, which may be expected to dissociate salts of polycations with polyanions, extract nucleoproteins from a variety of nuclei (Pollister and Mirsky, 1946; Mirsky and Pollister, 1946). The splitting of the basic proteins from DNA under these conditions has been demonstrated by dialyzing them out (Mirsky and Pollister, 1946), and by ultracentrifugation and electrophoresis (Cohen, 1945; Stern and Davis, 1946; Petermann and Lamb, 1948; Stern, 1949). Later studies indicate that this splitting may not occur at once in fresh preparations (Shooter, 1954). Either the nucleic acid or the histone moieties may be displaced from isolated nuclei by substances possessing a higher charge density. Thus heparin may displace DNA (Anderson and Wilbur, 1950, 1952; Roberts and Anderson, 1951), and protamine may displace histone (Mirsky and Ris, 1950). X-ray-scattering evidence also points to the view that nucleoproteins exist as simple addition products (Riley and Arndt, 1953). It should be emphasized, however, that certain very obvious differences exist between nucleoproteins as they appear in the nucleus and nucleohistones formed by mixing the two purified substances. In 0.14 *M* sodium chloride, nucleohistone is insoluble (Mirsky and Pollister, 1946) and nuclei are somewhat shrunken, with evidence of internal structure. The nuclei, however, respond readily to changes in salt concentration, whereas the dense nucleohistone fibers respond very slowly. The difference may very well be that the histone in the nucleus occupies a characteristic position along the DNA chain, but in the artificial nucleohistone fiber the histone is randomly associated with the DNA. This view receives some

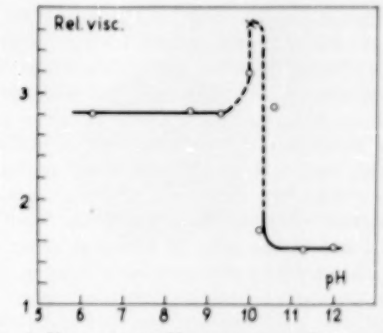

FIG. 4. VISCOSITY OF NUCLEOPROTEIN SOLUTIONS IN 1 *M* NaCl AS A FUNCTION OF *p*H
(From Frick, 1949).

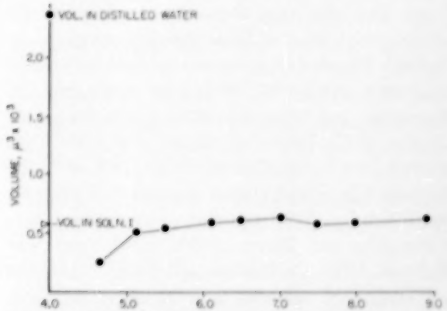

FIG. 5. EFFECT OF *p*H ON THE VOLUME OF ISOLATED RAT LIVER NUCLEI IN SOLUTIONS CONTAINING 0.023 *M* PHOSPHATE AND 0.145 *M* SUCROSE
(From Anderson and Wilbur, 1952).

confirmation from the work of Alexander (1953), who was able to prepare soluble DNA-protamine gels by allowing the two components to interact at extreme dilution. The suggestion was made that the protamine under these conditions attaches the DNA chains together end to end. A similar situation may well exist in the intact nucleus. Stern (1952) has considered that the spatial distribution of histone along the DNA chain is also of importance from a functional point of view. He suggests that histone contributes to the maintenance of a genetically important configuration of the DNA molecule, and that artificially recombined nucleohistone is an "artifact."

The nature of the linkages which hold the remaining protein (nonhistone) in the nucleus is not clear. The view that these are not held in the nucleus by virtue of their inability to pass out through the nuclear envelope has been previously presented (Anderson, 1953a; see comments by Hogeboom and Schneider, 1953; and by Stern and Mirsky, 1953). Rather, it appears that nonhistone protein may be linked to the DNA itself or to the histone. The complexing of a number of proteins by DNA has been reported (Greenstein, 1943; Greenstein and Hoyer, 1950; Goldwasser and Putnam, 1950; Geiduschek and Doty, 1952); the interaction of proteins such as serum albumin (Pederson, 1938) and insulin with basic proteins has long been known. In support of this concept, it should be noted that a variety of proteins can be adsorbed on isolated nuclei and displaced by other more basic proteins (Ohlmeyer et al., 1949; Ohlmeyer, 1950). A considerable amount of protein can also be removed from isolated nuclei by washing with saline (Dounce, 1950, 1952b; Stern and Mirsky, 1953; Kirkham and Thomas, 1953).

Assuming, therefore, that the "statistical chromosome" reflects the properties of a DNA-protein gelwork, the problem of chromosomal condensation then becomes essentially that of coiling up DNA molecules. Since changes in *p*H and simple salts sufficient to affect DNA coiling are not thought to occur in the dividing cell, the most probable mechanism remaining is one in which condensation is produced by polyvalent cations such as constrain the DNA in the nucleus —namely, histones, protamines, and similar basic substances. It is proposed that substances of this general class are usually related to the condensation of the chromosomes during prophase.

The essential characteristic of the general model presented here is that DNA chains are linked together at intervals by basic proteins, and that fairly long interhistone lengths of DNA exist. On both the histone and the DNA, nonhistone proteins are loosely held. In the "extended" state most of the DNA phosphate groups are not close to the positively charged groups of the histones. A number of slight changes may cause such a system to condense. Thus, if the loosely held protein is removed, the interhistone DNA segments will tend, at ionic strengths believed to obtain in the cell, to coil and cross-link with adjacent histone molecules so as to result in condensation or shrinkage. Similar results may be obtained by changes in the ionic character of the environment, or by the addition of *polycations*. In the light of the theory presented here, the key to the condensation mechanism is believed to be an increase in the latter.

Experimentally, the addition of small amounts of basic protein to isolated nuclei has a most profound condensing effect (Anderson, 1951), and only by the use of special techniques can chromosome-like bodies be condensed in isolated rat liver nuclei by polycations. The chromosomes seen in Fig. 6 were condensed by the addition of the dibasic amino acid, arginine.

It should be noted that the changes required to condense chromosomes may be somewhat less than might be supposed. If the system described is permeated by a solution of slightly acidic proteins (at cellular *p*H's most tissue proteins are on the alkaline side of their isoelectric points), it is evident that part of the reason for the noncontraction is the very presence of this acid protein which may reversibly associate with the nucleohistone. The acid protein serves to alter the polyelectrolyte balance in favor of the polyanions. Now if, through a small increment in polycation concentration, the chromosomal volume is decreased slightly, less of the permeating acidic protein will be contained in the gel, and a still further decrease in volume will result. Thus, it appears that swelling in a solution of cytoplasmic proteins may, since more of the protein is now in the gel, promote further swelling. Condensation, on the other hand, with consequent loss of such protein, may promote further contraction. If properly balanced, such a system could show an almost isoenergetic volume change. It makes little difference whether the added polycation attaches itself to the acidic protein or to the DNA chains, since it appears that sufficient histone is usually present in the nucleus to condense the DNA.

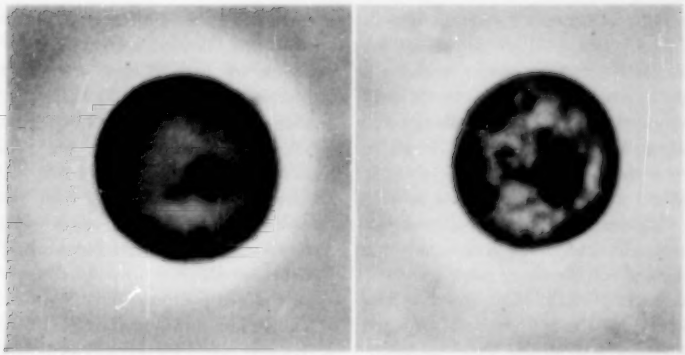

FIG. 6. LEFT, ISOLATED RAT LIVER NUCLEUS IN SALT-SUCROSE SOLUTION USED FOR NUCLEAR ISOLATION RIGHT, AFTER TREATMENT WITH 0.2 *M* ARGININE
(From Wilbur and Anderson, 1951).

Vendrely and Vendrely (1953) suggest that one arginine per DNA phosphate group is present in many nuclei. The amount of basic protein per nucleus in a given tissue is rather uniform (Alfert and Geschwind, 1953), but need vary only slightly to produce condensation or extension.

Stated somewhat differently, the volume occupied by chromatin material is thought to be controlled by competition between acidic and basic proteins or other polycations for sites on the nucleohistone. When the balance between these competing substances is shifted slightly in favor of the polycations, the DNA chains may now coil, with more of the surface of the DNA and histone molecules becoming available for mutual association. The net result would be (1) a loss from the chromatin of a large part of the proetin associated with it in the interphase nucleus, and (2) a decrease in volume.

As shown by Caspersson (1950), *the most marked change which occurs during prophase is a decrease in the amount of protein in the nucleus. The protein which remains is rich in arginine* (Serra, 1947) *and represents most of the basic protein of the cell* (Alfert and Geschwind, 1953).

Dounce (1952) has suggested that the DNA and histone are not present as a simple salt in the nucleus, since not all of the DNA phosphate is complexed with histone in the interphase nucleus. The structure proposed here would account for this.

Inasmuch as isolated nuclei can be made to show large volume changes, depending on the ionic character of the environment, it was suggested that variations in nuclear volume seen in various tissues and organs of the same animal could possibly be due to differences in the ionic composition of the intracellular fluid of the several types of cells (Anderson and Wilbur, 1952). However, further studies on isolated nuclei from several different organs (brain, kidney, and liver) of the rat showed that, when these were suspended in identical solutions, they maintained approximately the same relative size ratios found in fixed tissues. These differences persisted even when the nuclei were made to swell and shrink by appropriate changes in the suspending medium. The volume of the intracellular nucleus appears, therefore, to reflect both the ionic composition of the cell (which is probably rather similar in most tissues of the same animal) and the molecular organization of the nucleus itself. It has been shown that the protein content of many nuclei is proportional to the nuclear volume (Leuchtenberger and Schrader, 1951). If the nucleus is considered as largely made up of strands of DNA interlinked and probably cross-linked by histone, it is evident that the amount, charge density, and disposition of the histone would set some upper limit for the degree of swelling of such a system, short of complete dissolution. The nonhistone protein would be adsorbed on the unoccupied surfaces of the DNA and histone or would remain in solution in the interstices. Since the nuclear envelope is permeable to soluble cell proteins (Anderson, 1953a), it would be expected that the quantity of the protein inside the nucleus would bear a rather constant relation to the volume of the nucleus. Also, if cytoplasmic proteins tended to be very acid, the nuclei might tend to be large, and if more basic, would tend to be smaller. There is work on soluble tissue proteins which shows that the more basic soluble proteins are

present in lower concentrations in certain tumors (Sorof and Cohen, 1951). Although exceptions exist, it should be noted that tumor nuclei are generally larger than normal tissue nuclei (Miyaji, 1952). This increase in volume is not always due to an increase in ploidy. These considerations support the view that the volume of the somatic cell nucleus reflects a differentiation in the properties, amount, and distribution of basic proteins, and in the charge and concentration of nonhistone nuclear proteins and soluble tissue proteins.

In regard to the functions of histones other than their purely structural ones, it has been proposed that certain histones are specific gene inhibitors and differ in different tissues (Stedman and Stedman, 1950, 1951), a view supported by differences in the electrophoretic mobility of histones. Differentiation, from this point of view, would consist in the inhibition of a certain pattern of genes. Danielli (1953) has proposed that histones may act as inhibitors of protein synthesis generally, by virtue of their affinity for nucleic acids. This is a somewhat more general statement of the view proposed by the Stedmans. If the amount of histone is greater in an inactive gene than in an active one, it might be expected that the inactive gene would occupy a smaller volume. This problem may well be approached by the study of variations in the volume occupied by specific chromosome bands in cells of different organs. These are known to vary (Kosswig, 1948; Beermann, 1952). The concept that an inactive gene occupies a smaller volume than an active one supplies a clue to the mechanism behind the generalization that nuclear volumes vary with cell size. If the cytoplasm is considered as being in equilibrium with the nucleus (Anderson, 1953a), then a nucleus containing more active genes could maintain a larger volume of cytoplasm.

Additional support for the idea that the degree of condensation of DNA controls its activity comes from studies on heterochromatin, which may be considered as material remaining in the condensed state during interphase. When genes of euchromatic regions of the chromosome come into the neighborhood of heterochromatin by crossing over, their manifestation is lost (Prokofyeva-Belgovskaya, 1948; E. B. Lewis, 1950) or changed from dominant to recessive (McClintock, 1950). The same genes which in one species, sex, or tissue behave as heterochromatin in another may behave as euchromatin (Darlington, 1947), so as to suggest a relation between condensation and differentiation. It is possible that much of Darlington's work on so-called "nucleic acid starvation" and "overcharging" of chromosomes may be reinterpreted in terms of "undercondensation" and "overcondensation" of a relatively constant amount of DNA. If, as proposed here, the condensing basic proteins also cross-link adjacent DNA strands, then an excess of basic protein might tend to cross-link DNA strands in adjacent chromosomes. This would explain the stickiness observed between heterochromatic segments, and between so-called "overcharged" chromosomes.

The coiling and uncoiling of DNA in the chromosome is based on the assumption that segments of the chain exist which are not firmly or permanently bound to specific proteins or other substances. If DNA serves as a template for protein synthesis (Dalgliesh, 1953; Gamow, 1954; Dounce, 1952a; Campbell and Work, 1953), it would be expected that the length of the template would bear some relation to the unrolled length of the protein chain. In an average protein having a molecular weight of about 70,000, the combined chain length of the polypeptide chains would be approximately 2100 Å, assuming 3.5 Å per amino acid residue and an average amino acid molecular weight of 117. A DNA molecule of similar length would have a molecular weight of approximately 195,000 based on an assumed average nucleotide weight of 325 and an internucleotide distance of 3.5 Å. If DNA exists as a two-stranded coil (Watson and Crick, 1953), then a template of similar length would have slightly more than twice this molecular weight. A DNA molecule having a molecular weight of six million would then have the same length as a polypeptide chain of approximately one million molecular weight. It is therefore evident that the average DNA molecule could consist of more than one uncross-linked template segment and still be cross-linked with histone.

The length of the DNA molecule is of considerable importance in any consideration of the mechanism of chromosomal condensation from quite another point of view, since, in general, the longer a molecule is, the more likely it is to condense on itself.

The mechanism for chromosomal condensation proposed involves the coiling or kinking of DNA molecules. This coiling or condensation may be effective in itself in separating the daughter molecules formed by the autoduplication of DNA. The single DNA chain would be much less stiff

than the double coiled strand proposed by Watson and Crick (1953), and more easily compacted. Thus, the double-strand state may be more characteristic of interphase, whereas the single-strand condition may prevail during mitosis.

In connection with the effects of basic proteins on the volume of DNA-protein gels, it is of interest to note that the smallest and most basic proteins, the protamines, are found only in sperm nuclei, where space is most certainly at a premium, and where any mechanism for compacting genetic material would be expected to find its most highly developed expression.

To this point chromosome condensation has been treated in terms of the extension and condensation of a nucleoprotein gelwork without considering the fine structure of the chromosome. Unfortunately there has been little agreement as to what the ultrastructure of the chromosome really is, although it has been often concluded that the chromosome is held together by some type of continuous thread-like structure or chromonema. This "continuous skeleton" was thought by Serra (1947) to be of nonbasic protein with the nucleoprotein attached at intervals. The residual tryptophane-containing protein left after removal of histone and DNA was somewhat similarly considered by Mirsky and Ris (1947a and b). If histone is removed by acid treatment, or if DNA is digested away with DNAase (Mazia and Jaeger, 1939; Mazia, 1941 Catcheside and Holmes, 1947; McDonough, Rowan, and Mohn, 1952) the structural integrity of the chromosome is not destroyed. If both DNA and histone are removed, only very small coiled fragments composed of residual protein remain (Mirsky, 1951). But the "residual chromosomes" of Mirsky and Ris (1947a), obtained after extraction of thymus "chromosomes" in bulk with 1 *M* sodium chloride, are not seen when the same structures are similarly treated while being observed under the phase contrast microscope (Pollister, 1952). It is possible that the "residual chromosomes" are actually nuclear envelope material which has been stretched out during the course of nuclear rupture by high shearing forces. The existence and composition of a chromosomal backbone is therefore not a settled matter.

Both DNA and histone appear to have a non-uniform distribution on the chromosome. It cannot be assumed that DNA is absent from any region of the chromosome, however, since cytological methods can detect this substance only in comparatively high concentrations. Since DNA in crude preparations in a concentration hundreds of times lower than that seen in rat liver nuclei (50 mg./liter, for example) can produce a very high anomalous viscosity (Anderson, 1953c), concentrations of DNA below the limits of cytological detection may still have a structurally important effect. In these preparations cross links between parallel nucleoprotein strands are thought to be disrupted, while stronger bonds linking the molecules end-to-end remain.

Concepts of the association of DNA with a chromosomal backbone have been based, in many instances, on the following dubious generalizations: (1) that DNA varies in quantity during division in such a manner as to bear no relation to the number of chromosomes, chromomeres, or genes present; (2) that the amount of DNA on the chromosome could be varied experimentally, producing so-called "nucleic acid starvation" (Darlington, 1947); (3) that DNA moves off and onto the chromosomes during telophase and prophase with a possible accompanying change in polymerization (Darlington and Mather, 1950); (4) that DNA is a non-specific substance incapable of sufficient specificities to account for genetic activity; and (5) that enzyme-digestion and salt-extraction experiments indicate the existence of a ground structure which does not contain DNA.

The concepts of the role of DNA have undergone a revolution with the application of quantitative microspectrophotometric techniques (reviewed by Swift, 1953). With few exceptions, the amount of DNA *in the nucleus* appears to be directly related to the number of chromosomes present (Vendrely and Vendrely, 1948, 1949; Ris and Mirsky, 1949a; Pollister, Swift, and Alfert, 1951). Biochemically, DNA appears to be one of the most stable substances present in the cell. No change in the amount of DNA per diploid nucleus is seen with a wide variety of experimental treatments. As a result, the quantitative determination of DNA in a tissue has been considered as a direct indication of the number of cells present. No evidence that DNA depolymerizes in tissues except as a result of irradiation (Limperos, 1951) or cell death (Leuchtenberger, 1950) has been presented. The suggestion of Darlington and Mather (1950) that changes in DNA polymerization occur during mitosis has no experimental basis. The results of two lines of evidence, one chemical and physical (Watson and Crick, 1953; Gamow, 1954) and the other biological, based on the transforming effects seen in bacteria (Avery, McLeod, and McCarty,

FIG. 7. A HELICAL POLYMER WITH VARIATION IN PITCH OF HELIX

Two stable configurations with different pitches are illustrated at the two ends of the molecule. (From Pauling, 1953).

1944; Zamenhof, Alexander, and Leidy, 1953), indicate that the DNA molecule is capable of the internal complexity required of a genetic unit. These considerations support the view that DNA is an essential constituent of the gene.

An approach to the problem of chromosome structure may be made through the use of displacement effects involving large molecules. These may be termed macromolecular metathetical reactions. An example is found in the effect of heparin on isolated nuclei. The highly charged heparin molecule competes with DNA for basic sites on the histone molecule. Since heparin is more strongly charged, DNA is displaced from some of the sites. The result is the rapid swelling of the nuclear constituents into a large gel-like mass. No microscopically visible proteins strands or chromonemata may be discovered inside the intact nuclear membrane. These and other lines of evidence, including the breakage of chromosomes by ionizing radiations and ultraviolet light, lead to the conclusion that the DNA and protein of the nucleus are bound together to form a structure which is not dependent for its integrity on any central structure or backbone. Rather, as concluded by Kaufmann, Gay, and McDonald (1950), *the whole chromosome must be considered as an integrated structure with no single structural element.*

Numerous views of chromosome structure have been presented which range generally between two types of structure on the molecular level. The first suggests that discrete, particulate gene loci exist which find expression in discrete particles (Muller, 1947) bonded together. These have been thought by Mazia (1954) to be approximately 4000 Å long and 200 Å wide. The second view is that the chromosome is a genetic continuum in which discrete functional particles cannot be defined (Goldschmidt, 1951). A corresponding structural representation would be a continuous DNA-protein gelwork or a system composed of very long strands in parallel array. Fundamentally, the particulate and non-particulate concepts involve the question of the existence of bonds of considerably different energies along the chromosome.

A structure composed of individual particles may be compacted by condensation within the particles or micelles, or by packing or rearranging the particles themselves. As pointed out by Crane (1950), particles which are similar often condense most easily as spiral structures. This follows from the principle that a helical structure results from the continued application of a general identity operation to an asymmetric element, and accordingly that the helix is to be considered as the simplest infinite aggregate of units. Pauling (1953) has applied this general principle to the aggregation of globular proteins (Fig. 7) and has suggested that such helices could exist in two stable states having different pitch. While condensation can be accounted for in such a system, other problems arise. The chief of these, in the case of a chromosome composed of a series of discrete particles loosely bound together (as contrasted to a long bundle of parallel strands), concerns the reduplication of the particles. The most plausible mechanisms for exact molecular reduplication involve reduplication of the individual linear molecules themselves without recourse to long-range forces or multistep syntheses. In dealing with the reduplication of a multimolecular particle the question arises whether all the molecules or simple histone-DNA chains are identical or not. If they are different, then some mechanism for sorting them out and dividing the particle into two identical ones must be considered.

A number of authors have reported evidence for the existence of fibers running parallel to the length of salivary gland chromosomes (Palay and Claude, 1949; Yasuzumi, Odate, and Ota, 1951). Beermann (1952) considers these strands to be wound into a loosely cabled spiral, with each strand extending the length of the chromosome. Ambrose, Cuckow, and Gopal-Ayengar (1952) reported the threads in *Chironomus* salivary glands to have a diameter of 100–200 Å. Observations with the polarization microscope (Schmidt, 1941; Ambrose and Gopal-Ayengar, 1952) indicate that the long nucleoprotein molecules are arranged approximately parallel to the axis of the chromosome.

On the basis of these and other findings, Ambrose (1956) has proposed the following model of the

structure of the salivary gland chromosome. All structures are parallel to the long axis:

(1) Nucleic acid and protein chains with a diameter of 15–20 Å. These are inferred from x-ray and optical effects.

(2) Bundles of these chains arranged to form microfibrils 100–200 Å in diameter. Observable in the electron microscope.

(3) The microfibrils are arranged in bundles to form the chromonemata with a diameter of 5000–10,000 Å. These may be observed with the light microscope.

(4) Bundles of chromonemata form the salivary gland chromosome, which may have a diameter up to 20 μ.

The microfibrils may actually be formed from sections 3000–4000 Å in length which are held together by secondary forces (Mazia, 1954; Ambrose, 1956). The nucleoprotein-protein chains could therefore be continuous the entire length of the chromosome, but could have very weak links at points along the chain. If these weak links were identically spaced along the chains making up the microfibril, the microfibril would behave as if it were composed of long particles with a diameter of 100–200 Å. These particles are therefore in a sense artifacts of the isolation procedure. Such a model reconciles some of the contradictory views of chromosome structure which have been put forward previously, and is not at variance either with the concept that the chromosome contains discrete particulate gene loci (Muller, 1947), or that the chromosome is a genetic continuum in which discrete functional particles cannot be defined (Goldschmidt, 1951).

It is of interest that the available data can be used to construct a model which accounts for the structure of the extended and the condensed chromosome if the following assumptions are allowed:

(1) The ultimate genetic structure is a linear system, able to duplicate itself, and to engage in some other specific activity such as RNA or protein synthesis.

(2) The ultimate linear structure is based on the DNA molecule, probably interlinked end to end by protein. This structural unit may contain information for several genetic effects and is not necessarily synonymous with the gene.

(3) The linear structure is not single, but is composed of a number of similar, generally parallel, strands which form a loose skein in the extended state.

(4) The molecular strands or chains are identical in *all* respects, including the structure and orientation of protein attached to the strands.

(5) Condensation involves a change in affinity between adjacent strands such as would occur on the unmasking of basic charges on the histone molecule, the addition of small polycations, etc.

(6) In the resting or extended condition the chains forming the skein are *very* loosely cross-linked, and such linkages as occur are rather widely separated.

(7) Identical molecular chains or strands condense against each other best by moving parallel to one another a sufficient distance to allow non-identical segments to condense.

The first assumption might be justified on the basis of economy of ideas and simplicity. The second is based partly on data previously listed. The concept that one DNA molecule may be part of more than one gene deserves comment, however. Kurnick and Herskowitz (1952) calculated that a haploid set of Drosophila salivary chromosomes contains 44,000 DNA molecules if a molecular weight of 10^6 is assumed. If the number of genes is taken as approximately 5,000, then about nine DNA molecules per gene would be present. But if the molecular weight is taken as being around 8×10^6, then the ratio would be nearly that of one gene per DNA molecule. However, the finding that two transforming activities may exist in the same DNA molecule in experiments with pneumococcus (Hotchkiss and Marmur, 1954) argues against the "one gene, one DNA molecule" concept. It does not appear that any data are at present available from which the number of duplications (the number of identical molecular strands) can be calculated. The stability of the genetic mechanism argues in favor of a multiple-strand system, with some process for intercomparison and elimination of strands or sections of strands which do not match the rest. The necessity for such "inspection systems" has been discussed by Crane (1950). If the chromosome was built up from only one long strand in which DNA played a major role, it would be difficult to see how chromosome stickiness, which is thought to be due to loose DNA segments, could occur without chromosome breakage.

If one takes the available data at face value, the overall statistical model arrived at is that of a skein of DNA chains, each chain being approximately 20 Å in diameter, and between 5 to 40×10^6 Å long. The associated histone molecules

(data from Davison, James, Shooter and Butler, 1954, for thymus histone) appear to be of two types: one of low molecular weight (18,000) and a high axial ratio (1:28); the other much larger, with a molecular weight of 35,000. If the dimensions of the smaller molecule are calculated as described by Neurath (1939) they are found to be 11.6 and 319 Å. This can only be true if the molecule exists as an essentially linear polypeptide chain. As pointed out by Watson and Crick (1953), "... we know almost nothing about the structural features of protamines and histones. Our only clue is the finding of Astbury (1947) and of Wilkins and Randall (1953) that the x-ray pattern of nucleoprotamine is very similar to that of DNA alone. This suggests that the protein components or at least some of it, also assumes a helical form and in view of the very open nature of our model we suspect that proteins form a third helical chain between the pair of polynucleotide chains. As yet nothing is known about the function of the protein; perhaps it controls the coiling and uncoiling and perhaps it assists in holding the single polynucleotide chains in a helical configuration." The low molecular-weight histones would be admirably suited for this function in view of their threadlike configuration. From calculations based on the amount of this smaller histone in thymus nuclei and the amount of DNA present, it can be shown that the sum of the lengths of these small histone molecules is almost twice the sum of the lengths of the DNA chains. The larger histone molecules appear to be spaced along the DNA chains at average distances of about 700 Å.

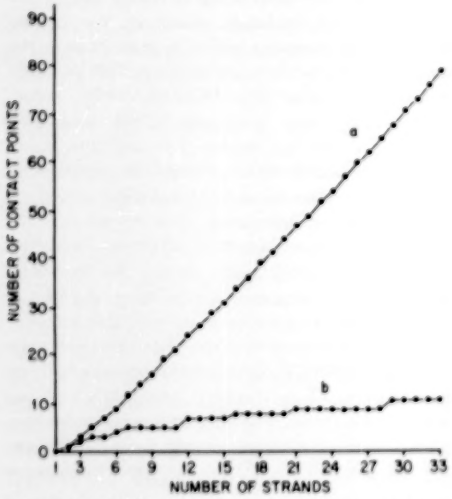

FIG. 8. TOTAL NUMBER OF CONTACT POINTS BETWEEN STRANDS IN A HELIX OBSERVED IN A THIN SECTION PERPENDICULAR TO THE AXIS AS A FUNCTION OF THE NUMBER OF STRANDS (CURVE *a*).

The number of such contact points which must be broken to separate the strands into two groups, as evenly matched as possible (Curve *b*).

It follows from the identical configuration of adjacent chains that they would not tend to condense in a parallel fashion (DNA against DNA, large histone molecule against large histone molecule), although conceivably some interaction between the smaller histone molecules in one strand and the DNA in another might occur. The simplest scheme for condensing identical chains is for each to be displaced parallel to its axis a sufficient distance to allow non-identical segments to condense, i.e., large histone molecule with DNA. The only way in which this can occur efficiently in a system where longitudinal translation of alternate molecules is prevented is by the formation of a helix. The distance which each strand moves relative to its neighbors will determine the pitch of the helix.

If one considers a very long skein of strands, it is evident that if a helix forms in one part of the bundle, twisting in the opposite direction will occur on either side of the segment where the original helix formed, giving three segments which alternate in direction of twist. (Coiling of the molecular strands described here should not be confused with the helical structure of DNA itself.) It can be easily shown that stresses will be set up between loosely cross-linked chains at the site where the direction of twist changes. The magnitude of the forces tending to split the chains away from each other at this point will be proportional to some function of the number of junction points between neighboring chains. This number increases rapidly as the number of chains increases, while the number of such contact points which must be broken to separate the skein into two smaller skeins increases at a much slower rate as the number of strands in the skein is increased. This is shown in Fig. 8, where the number of contact points between strands observed in a thin section perpendicular to the axis of a twisted cable, and the number of such contact points which will be broken when the strands are separated into two nearly equal groups, are plotted against the total number of strands. With seven strands, twelve contact points will exist, five of which are broken when the cable is divided into two groups with

four in one and three in the other. If the cable has fourteen strands, however, twenty-nine junctions points will exist, while only seven need be broken. It is evident that a number of strands N can be chosen such that it can be twisted in alternate directions at intervals (assuming a certain bonding energy between adjacent strands), while an attempt to do the same thing with twice this number ($2N$) will produce shearing forces sufficient to cause the skein to form two parallel helices. This mechanism, shown schematically in Fig. 9, is proposed as the origin of the division of the chromosome. As the coiling of the skein proceeds, the original $2N$ helix segment is untwisted and recoiled into two helices.

Further condensation produces more segments, each twisted in alternate direction. Unless the number of strands in the $1N$ skein is less than five, or unless a hollow tube is produced, a number of unresolved forces exist. For example, a seven-strand system with one strand in the center surrounded by six others has no provision for shortening the center strand as the others coil about it. The probability therefore exists that the original molecular coil will form a second tight coil in an attempt to resolve these forces, and may also form larger coils. While it is not possible to make any very accurate approximation of the size of the various coils, the second coil is of the same magnitude as the subminor coil of a small chromosome.

It is apparent that this model allows for the reduplication of single molecular strands in an uncoiled condition, separation of these into two skeins of strands coiling at intervals in opposite directions and the further coiling of the separate skeins into more complex higher order coils. It does not require reduplication of large beaded structures by long range forces, the separation of coiled systems by extensive breaking and rejoining, or the spiralization of long structures where the free ends would be required to rotate at a high rate of speed, as might be the case if the original skein were twisted in one direction along its entire length. The alternation of direction occurring in the first or molecular coil might suggest that the direction of coiling of the larger, microscopically visible coils would be indeterminate. Actually there is no reason (or space for that matter) for the interphase chromosome to uncoil completely. Rather, it will retain part of the same spiral structure of the condensed chromosome. When condensation with twist reversal at the molecular level occurs,

FIG. 9. A MODEL OF A CHROMOSOME CONSISTING OF LONG STRANDS OF NUCLEOPROTEIN

In the extended state (lower left) very little cross-linking exists. As an attempt is made to condense this system, with the restriction that identical segments of the chains cannot condense immediately next to each other, a helix altering in direction of twist at intervals is produced (upper left). Stresses set up at the point of twist reversal separate the skein into two bundles (upper center and right center). The two bundles form separate helices which coil further to produce the second and third coils shown (center and lower right). While the original bundles exhibit twist reversal along their entire length, the larger coils rarely do so because of their stiffness.

segments of the skein may attempt to form larger (subminor) coils going in opposite directions. For reasons of stiffness and efficiency of packing these will tend to revert to the one direction which is predominant. If 50 per cent of the length of the skein attempts to produce a second coil in one direction, and 50 per cent coils the other way, the interplay of forces will be resolved in terms of that small amount of coiling remaining from the previous condensation cycle. It would be expected, therefore, that the direction of coiling would be rather constant, but reversal of direction along part or all of the chromosome should be occasionally observed, as is indeed the case (Manton, 1950).

It is not unlikely that the points where twist reversal occurs are the points of rupture when the chromosome is broken down, as in the distilled water extractions of Mazia (1954). A coil of the dimensions of the second coil shown in Fig. 9 has

been shown in an electron micrograph by Frajola, Greider, and Rabatin (1954).

This condensation mechanism, by condensing only identical strands, may serve to eliminate those which are different, damaged, or defective. The stability of genetic patterns through tens of thousands of reduplications may well be due to such an intercomparison and defect-elimination system. The rujevenating effect of cell division (or conversely the lack of aging effects in cells which continue to divide) may well be due to this mechanism.

In considering the relation of microscopic observation to the problem of chromosomal condensation it should be noted, first, that most concepts and models of chromosome structure are largely derived from the study of giant non-condensing chromosomes, and second, that the problem of fixation alterations in chromosomal material is still far from being solved.

It is the purpose of the remainder of the papers in this series to show that the simple mechanism involving cyclical variations in the relative amounts of polymerized acidic and basic groups (shifts in polyelectrolyte balance) occurring in a loosely organized nucleic-acid–protein gelwork, and which are thought to be causally related to the division of primordial cells, may be extended to explain a number of other aspects of mitosis seen in contemporary life.

The pessimistic views concerning the complexity of mitosis and the difficulties attendant on any studies seeking to supply solutions to the problems involved, which have been expressed by Schrader (1953), undoubtedly represent a mature and realistic evaluation of the present status of the field. The large cytological literature appears to contain instances which may be cited as evidence against almost any conceivable detailed theory of cell division. It may be well to inquire, therefore, into the justification of an approach such as is presented in this series.

If a science is made up of those hypotheses which have not yet been discarded, then the history of a science is the history of hypotheses. Each new hypothesis or generalization at the outset lacks the pertinent experimental data for its proper evaluation and delimitation. Only by exploring an idea thoroughly, by pushing it as far as it will go, can such an evaluation be obtained. A case in point is the history of the study of pH in biological materials. Only after a long series of heated debates and claims that pH controlled a variety of processes ranging from aging to the determination of the sex of human offspring, has the whole matter fallen into proper perspective. The present evaluation rests on a mass of experimental data, which in turn owes its existence to a number of theories, some of which are now merely amusing.

The object here is to present a point of view which will stimulate a line of approach to the problem of cell division. The justification for such an endeavor lies not in that a theory may prove to be correct, partially correct, or even slightly correct. Rather, a theory is justified by the experimental data which it serves to generate.

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LIST OF LITERATURE

ALEXANDER, J. 1948. *Life, Its Nature and Origin.* 291 pp. Reinhold, New York.

ALEXANDER, P. 1953. The combination of protamine with desoxyribonucleic acid. *Biochim. biophys. Acta,* 10: 595–599.

——, and S. F. HITCH. 1952. A comparative study of the anomalous viscosity of a high molecular weight polyelectrolyte and thymus nucleic acid. *Biochim. biophys. Acta,* 9: 229–236.

ALFERT, M., and I. I. GESCHWIND. 1953. A selective staining method for the basic proteins of cell nuclei. *Proc. nat. Acad. Sci., Wash.,* 39: 991–999.

AMBROSE, E. J. 1956. The structure of chromosomes. *Prog. Biophys. biophys. Chem.,* 6: 25–55.

AMBROSE, E. J., F. W. CUCKOW, and A. R. GOPAL-AYENGAR. 1954. Chromosome structure. Int. Cytol. Congr., Leiden., Publ. under I.U.B.S.

AMBROSE, E. J., and A. R. GOPAL-AYENGAR. 1952. Molecular organization in giant chromosomes. *Nature, Lond.,* 169: 652–653.

ANDERSON, N. G. 1951. Studies on isolated mammalian somatic cell nuclei. Thesis. Duke University, Durham, N. C.

——. 1952. The effect of various enzymes on nuclei isolated from rat liver. *J. Tenn. Acad Sci.,* 27: 198.

——. 1953a. On the nuclear envelope. *Science,* 117: 517–521.

——. 1953b. Studies on isolated cell components.

VI. The effects of nucleases and proteases on rat liver nuclei. *Exp. Cell Res.*, 5: 361–374.

ANDERSON, N. G. 1953c. Degree of polymerization of deoxyribonucleic acid. *Nature, Lond.*, 172: 807–808.

——, and K. M. WILBUR. 1950. Release of nucleic acids from cell components by heparin. *Fed. Proc.*, 9: 254.

——, and ——. 1950. Studies on isolated cell components. II. The release of a nuclear gel by heparin. *J. gen. Physiol.*, 34: 647–656.

——, and K. M. WILBUR. 1952. Studies on isolated cell components. IV. The effect of various solutions on the isolated rat liver nucleus. *J. gen. Physiol.*, 35: 781–796.

ASTBURY, W. T. 1939. The x-ray study of proteins and related structures. *Sci. Progr.*, 34: 1–19.

——. 1947. X-ray studies of nucleic acids. *Symp. Soc. exp. Biol.*, 1: 66–76.

AVERY, O. T., C. N. MACLEOD, and M. MCCARTY. 1944. Studies on the chemical nature of the substance inducing transformation of pneumococcal types. Induction of transformation by a desoxyribonucleic acid fraction isolated from pneumococcus type III. *J. exp. Med.*, 79: 137–158.

BALAZS, A., and H. HOLMGREN. 1949. Effect of sulfomucopolysaccharides on growth of tumor tissue. *Proc. Soc. exp. Biol., N. Y.*, 72: 142–145.

BANK, O. 1941. Der Zellkern als Komplexkoazervat. *Protoplasma*, 35: 419–461.

BARRON, E. S. G. 1954. The effect of x-rays on systems of biological importance. In *Radiation Biology* (Alexander Hollaender, ed.), Vol. I, pp. 283–314. McGraw-Hill, New York.

BARNUM, C. P., R. A. HUSEBY, and H. VERMUND. 1953. A time study of the incorporation of radiophosphorus into nucleic acids and other compounds of a transplanted mouse mammary carcinoma. *Cancer Res.*, 13: 880–889.

BARTH, L. G. 1929. The effects of acids and alkalies on the viscosity of protoplasm. *Protoplasma*, 7: 505–534.

BARTON, A. D. 1954. Evidence for the biochemical stability of desoxyribonucleic acid (DNA). *Fed. Proc.*, 13: 422.

BASU, S. 1951. Viscosity of sodium thymonucleate. *Nature, Lond.*, 168: 341–342.

BATAILLON, E. 1929. Analyse de la fécondation par la parthénogénèse expérimentale. *Arch. Entw-Mech. Org.*, 115: 707–778.

BECK, L. V., and H. SHAPIRO. 1936. Permeability of germinal vesicle of the starfish egg to water. *Proc. Soc. exp. Biol. N. Y.*, 34: 170–172.

BEERMANN, W. 1952. Chromomerenkonstanz und spezifische Modifikationen der Chromosomenstruktur in der Entwicklung und Organdifferenzierung von *Chironomus tetans*. *Chromosoma*, 5: 139–198.

BERNAL, J. O. 1951. *The Physical Basis of Life*. 80 pp. Routledge and Kegan Paul, London.

BERNSTEIN, M. H., and D. MAZIA. 1953. The desoxyribonucleoprotein of sea urchin sperm. I. Isolation and analysis. *Biochim. Biophys. Acta*, 10: 600–606.

BLOCH, D. P., and G. C. GODMAN. 1955. A microphotometric study of the synthesis of desoxyribonucleic acid and nuclear histone. *Biochem. biophys. Cytol.*, 1: 17–28.

BLOOM, W. L., and F. G. BLAKE. 1948. Studies on an antibacterial polypeptide extracted from normal tissues. *J. infect. Dis.*, 83: 116–123.

BLUM, H. F. 1951. *Time's Arrow and Evolution*. 222 pp. Princeton Univ. Press, Princeton.

BRAGG, L. 1954. X-ray studies of biological molecules. *Nature, Lond.*, 174: 55–59.

BRUNISH, R., and J. M. LUCK. 1952. Amino acid incorporation in vivo into liver fractions. *J. biol. Chem.*, 198: 621–628.

BULLOUGH, W. S. 1952. The energy relations of mitotic activity. *Biol. Rev.*, 29: 133–168.

BUNGENBERG DE JONG, H. G. 1949a. Morphology of coacervates. In *Colloid Science*, Vol. 2 (H. R. Kruyt, ed.), pp. 433–482. Elsevier, New York.

——. 1949b. Reversal of charge phenomena, equivalent weight and specific properties of the ionised groups. In *Colloid Science*, Vol. 2 (H. R. Kruyt, ed.), pp. 259–334. Elsevier, New York.

CALLAN, H. G. 1949. A physiological study of isolated nuclei and its implications regarding gene action. *Proc. 8. int. Congr. Genet., Stockholm, 1948, Hereditas*, suppl. vol., 547–548.

CALVIN, M. 1956. Chemical evolution and the origin of life. *Amer. Scient.*, 44: 248–263.

CAMPBELL, P. N., and T. S. WORK. 1953. Biosynthesis of proteins. *Nature, Lond.*, 171: 997–1001.

CARLSON, J. G., A. HOLLAENDER, and M. E. GAULDEN. 1947. Ultraviolet radiation as a means of sterilizing tissue culture materials. *Science*, 105: 187.

CASPERSSON, T. O. 1950. *Cell Growth and Cell Function*. 185 pp. Norton, New York.

CATCHESIDE, D. G., and B. HOLMES. 1947. The action of enzymes on chromosomes. *Symp. Soc. exp. Biol.*, 1: 225–231.

CHAET, A. B. 1952. The action of heparin preparations on cells and tissues. *Biol. Bull., Woods Hole*, 103: 281.

CHAMBERS, R. 1917. Microdissection studies. II. The cell aster: A reversible gelation phenomenon. *J. exp. Zool.*, 23: 483–504.

——. 1951. The formation of the aster in artificial parthenogenesis. *J. gen. Physiol.*, 4: 33–39.

——, and M. BLACK. 1941. Electrolytes and

nuclear structure of the cells of the onion bulb epidermis. *Amer. J. Bot.*, 28: 364–371.

CHURNEY, L. 1941. *Cytology, Genetics, and Evolution.* In *Univ. Penn. Bicentennial Conf.*, Univ. Penn. Press, Philadelphia.

——. 1942. The osmotic properties of the nucleus. *Biol. Bull., Woods Hole*, 82: 52–67.

COHEN, S. S. 1945. The enzymatic degradation of thymus nucleohistone. *J. biol. Chem.*, 158: 255–264.

CRANE, H. R. 1950. Principles and problems of biological growth. *Sci. Monthly*, 70: 376–389.

DALGLIESH, C. E. 1953. The template theory and the role of transpeptidation in protein biosynthesis. *Nature, Lond.*, 171: 1027–1028.

DALY, M. M., A. E. MIRSKY, and H. RIS. 1950. The amino acid composition and some properties of histones. *J. gen. Physiol.*, 34: 439–450.

DANGEARD, P. 1947. Cytologie végétale et cytologie générale. In *Encycl. biol.*, Vol. 26 (P. Lechevalier, ed.), pp. 1–611. Paris.

DANIELLI, J. F. 1951. The cell surface and cell physiology. In *Cytology and Cell Physiology* (G. Bourne, ed.) pp. 150–182. Clarendon Press, Oxford.

——. 1953. *Cytochemistry: A Critical Approach.* 139 pp. John Wiley & Sons, New York.

DAOUST, R., F. D. BERTALANFFY, and C. P. LEBLOND. 1954. The rates of desoxyribonucleic acid synthesis and mitosis in lung. *J. biol. Chem.*, 207: 405–410.

DARLINGTON, C. D. 1947. Nucleic acid and the chromosomes. *Symp. Soc. exp. Biol.*, 1: 252–269.

——, and K. MATHER. 1949. *The Elements of Genetics.* 446 pp. Macmillan & Co., New York.

DAVISON, P. F., D. W. F. JAMES, K. V. SHOOTER, and J. A. V. BUTLER. 1954. The histones of calf thymus deoxyribonucleoprotein. II. Electrophoretic and sedimentation behavior and a partial fractionation. *Biochim. biophys. Acta*, 15: 415–424.

DOUNCE, A. L. 1950. Enzyme systems of isolated cell nuclei. *Ann. N. Y. Acad. Sci.*, 50: 982–997.

——. 1952a. Duplicating mechanism for peptide chain and nucleic acid synthesis. *Enzymologia*, 15: 251–258.

——. 1952b. The enzymes of isolated nuclei, in the chemistry and physiology of the nucleus. *Exp. Cell Res.*, 2, Suppl.: 103–122.

DURYEE, W. R. 1937. Isolation of nuclei and non-mitotic chromosome pairs from frog eggs. *Arch. exp. Zellforsch.*, 19: 171–176.

FELIX, K., H. FISCHER, A. KREKELS, and R. MOHR. 1951. Nucleoprotamin. I. *Hoppe-Seyl. Z.*, 287: 224–234.

——, J. HARTLEIB, and A. KREKELS. 1952. Nucleoprotamin. IV. *Hoppe-Seyl. Z.*, 290: 66–69.

——, and A. KREKELS. 1953. Diamino Säuren einiger Protamin. *Hoppe-Seyl. Z.*, 295: 107–109.

FISCHER, A. 1936. Über die Wirkung des Heparins auf das Wachstum von Gewebezellen in Vitro. *Protoplasma*, 26: 344–350.

FRAJOLA, W. J., M. H. GREIDER, and J. G. RABATIN. 1954. Electron microscopy of calf thymus nucleoprotein. I. Effect of hydrochloric acid and deoxyribonuclease. *Biochim. biophys. Acta*, 14: 18–25.

FRANKLIN, R. E., and R. G. GOSLING. 1953a. Evidence for 2-chain helix in crystalline structure of sodium deoxyribonucleate. *Nature, Lond.*, 172: 156–157.

——. 1953b. Molecular configuration in sodium thymonucleate. *Nature, Lond.*, 171: 740–741.

FREUNDLICH, H. 1937. Some recent work on gels. *J. phys. Chem.*, 41: 901–910.

FREY-WYSSLING, A. 1949. Physicochemical behavior of cytoplasm. *Research*, 2: 300–307.

FRICK, G. 1949. Some physico-chemical properties of thymo-nucleoprotein prepared according to Mirsky and Pollister. *Biochim. biophys. Acta*, 3: 103–116.

FURBERG, S. 1952. On the structure of nucleic acids. *Acta chem. scand.*, 6: 634–640.

GAMOW, G. 1954. Possible relation between deoxyribonucleic acid and protein structures. *Nature, Lond.*, 173: 318.

GEIDUSCHEK, E. P., and P. DOTY. 1952. A light scattering investigation of the interaction of sodium desoxyribonucleate with bovine serum albumin. *Biochim. biophys. Acta*, 9: 609–618.

GOERNER, A. 1931. The influence of anticlotting agents on transplantation and growth of tumor tissue. *J. Lab. clin. Med.*, 16: 369–372.

GOLDACRE, R. J. 1952. The folding and unfolding of protein molecules as a basis of osmotic work. *Int. Rev. Cytol.*, 1: 135–164.

——, and I. J. LORCH. 1950. Folding and unfolding of protein molecules in relation to cytoplasmic streaming, amoeboid movement, and osmotic work. *Nature, Lond.*, 166: 497–500.

GOLDSCHMIDT, R. B. 1951. The theory of the gene. *Cold Spr. Harb. Symp. quant. Biol.*, 16: 1–11.

GOLDSTEIN, L., and C. V. HARDING. 1950. Osmotic behavior of isolated nuclei. *Fed. Proc.*, 9: 48–49.

GOLDWASSER, E., and F. W. PUTNAM. 1950. Electrophoretic study of interaction of serum albumin thymus nucleic acid. *J. phys. Chem.*, 54: 79–89.

GOSSELIN, R. E., A. ROTHSTEIN, G. J. MILLER, and H. L. BERKE. 1952. The hydrolysis and excretion of polymeric phosphate. *J. Pharmacol.*, 106: 180–192.

GREEN, D. E. 1952. Organized enzyme systems. *J. cell. comp. Physiol.*, 39, Suppl. 2: 75–99.

GREEN, H. N., and H. B. STONER. 1950. *Biological*

Actions of the Adenine Nucleotides. 221 pp. H. K. Lewis & Co., London.

GREENSTEIN, J. P. 1943. The colloid osmotic pressure of mixtures of protein and thymus nucleate. *J. biol. Chem.*, 150: 107–112.

——, and M. L. HOYER. 1950. Effect of thymus nucleate on the thermal coagulation of albumin solutions. *J. biol. Chem.*, 182: 457–466.

GROSS, P. R. 1952. A study of colloidal changes in sea urchin egg homogenates. *Biol. Bull., Woods Hole*, 103: 293.

GULLAND, J. M., and D. O. JORDAN. 1947. The macromolecular behavior of nucleic acids. *Symp. Soc. exp. Biol.*, 1: 56–65.

HALDANE, J. B. S. 1933. *Science and Human Life*. 287 pp. Harper, New York.

HAMER, D., and D. L. WOODHOUSE. 1949. Amino acid composition of salmine. *Nature, Lond.*, 163: 689–690.

HARDING, D. 1949. Effect of heparin on artificial activation in the frog egg. *Proc. Soc. exp. Biol., N. Y.*, 71: 14–15.

——. 1951. Initiation of cell division in the *Arbacia* egg by injury substances. *Physiol. Zool.*, 24: 54–69.

HARVEY, E. B. 1940. A comparison of the development of nucleate and non-nucleate eggs of *Arbacia punctulata*. *Biol. Bull., Woods Hole*, 79: 166–187.

HARVEY, E. N. 1910. Methods of artificial parthenogenesis. *Biol. Bull., Woods Hole*, 18: 269–280.

HAUROWITZ, F. 1950. *Chemistry and Biology of Proteins*. 374 pp. Academic Press, New York.

HEILBRUNN, L. V. 1928. *The Colloid Chemistry of Protoplasm*. Protoplasma-Monographien, Vol. I. 356 pp. Gebr. Borntraeger, Berlin.

——. 1952. *An Outline of General Physiology*. Third edition. 818 pp. W. B. Saunders & Co., Philadelphia.

——, and W. L. WILSON. 1949. The effect of heparin on cell division. *Proc. Soc. exp. Biol. N. Y.*, 70: 179–182.

——, and ——. 1950. The prevention of cell division by anti-clotting agents. *Protoplasma*, 39: 389–399.

——, ——, and D. HARDING. 1951. The action of tissue extracts on cell division. *J. nat. Cancer Inst.*, 11: 1287–1298.

HERMANS, P. H. 1949. Gels. In *Colloid Science* (H. R. Kruyt, ed.), Vol. II, pp. 483–651. Elsevier Pub. Co., New York.

HERWERDEN, M. A. VAN. 1924. Umkehrbare Gelbildung in den Zellen eines mehrzelligen Organismus. *Biol. Zbl.*, 44: 579–582.

HOGEBOOM, G. H., and W. C. SCHNEIDER. 1953. On the nuclear envelope. *Science*, 118: 419.

HOLLAENDER, A., J. P. GREENSTEIN, and W. V. JENRETTE. 1941. Effects of ultraviolet radiation on sodium thymonucleate. *J. nat. Cancer Inst.*, 2: 23–28.

HOLMES, S. J. 1948. *Organic Form and Related Biological Problems*. 169 pp. Univ. Calif. Press, Berkeley.

HOROWITZ, N. H. 1945. On the evolution of biochemical syntheses. *Proc. nat. Acad. Sci., Wash.*, 31: 153–157.

HOTCHKISS, R. D., and J. MARMUR. 1954. Double marker transformations as evidence of linked factors in desoxyribonucleate transforming agents. *Proc. nat. Acad. Sci., Wash.*, 40: 55–60.

HUGHES, A. 1952. *The Mitotic Cycle*. 232 pp. Butterworths, London.

ISENBERG, I. 1953. Cell division by swelling stresses. *Bull. math. Biophys.*, 15: 73–82.

JEENER, R. 1946. Influence de la concentration ionique sur les gels de nucléohistone. *C. R. Soc. biol., Paris*, 140: 689–692.

JORDAN, D. O. 1950. The behavior of nucleic acids and polymeric electrolytes. *Trans. Faraday Soc.*, 46: 792–793.

——. 1952. Nucleic acids, purines and pyrimidines. *Annu. Rev. Biochem.*, 21: 209–244.

KAHLER, H., and B. J. LLOYD. 1953. The electron microscopy of sodium desoxyribonucleate. *Biochim. biophys. Acta*, 10: 355–359.

KASSEL, R., and M. J. KOPAC. 1950. Changes in the nucleus of *Amoeba proteus* following removal from the organism. *Anat. Rec.*, 108: 573.

KATER, J. M. 1927. Nuclear structure in active and hibernating frogs. *Z. Zellforsch.*, 5: 263–277.

——. 1928. Nuclear structure and chromosomal individuality. Somatic and germ nuclei of the rat. *Z. Zellforsch.*, 6: 587–610.

KAUFMANN, B. P. 1952. Cytochemical studies of the action of trypsin. I. Digestion of salivary-gland chromosomes. *Proc. nat. Acad. Sci., Wash.*, 38: 464–468.

——, H. GAY, and M. R. MCDONALD. 1950. Analysis of cell structure by digestion with enzymes. *Genetics*, 35: 117.

KIRKHAM, W. R., and L. E. THOMAS. 1953. The isolation of globulins from cellular nuclei. *J. biol. Chem.*, 200: 53–57.

KOPAC, M. J. 1951. Probable ultrastructures involved in cell division. *Ann. N. Y. Acad. Sci.*, 51: 1541–1546.

KOSSEL, A. 1928. *The Protamines and Histones*. Longmans, Green, and Co., New York.

KOSSWIG, C. 1949. Demonstration of preparations of salivary chromosomes of different tissues of Chironomus. *Proc. 8. int. Congr. Genet., Stockholm, 1948, Hereditas*, Suppl. Vol., 609–610.

KUHN, W., B. HARGITAY, A. KATCHALSKY, and H. EISENBERG. 1950. Reversible dilation and contraction by changing the state of ionization of

high-polymer acid networks. *Nature, Lond.*, 165: 514–516.

KUBNICK, N. B., and I. H. HERSKOWITZ. 1952. The estimation of polyteny in *Drosophila* salivary gland nuclei based on determination of desoxyribonucleic acid content. *J. cell. comp. Physiol.*, 39: 281–300.

LANDAHL, H. D. 1942a. A kinetic theory of diffusion forces in metabolizing systems. *Bull. math. Biophys.*, 4: 15–26.

——. 1942b. A mathematical analysis of elongation and constriction in cell division. *Bull. math. Biophys.*, 4: 45–62.

——. 1942c. An analysis of the shapes of a cell during division with particular reference to the role of surface tension. *Bull. math. Biophys.*, 4: 151–154.

——. 1943. A mechanism of division of a cell with an impermeable membrane. *Bull. math. Biophys.*, 5: 75–81.

LANHAM, U. N. 1952. Oparin's hypothesis and the evolution of nucleoproteins. *Amer. Nat.*, 86: 213–218.

LASKOWSKI, M., and D. RYERSON. 1943. The effect of different sodium chloride concentrations on nuclei from chicken erythrocytes. *Arch. Biochem.*, 3: 227–233.

LETTRÉ, H. 1952. Some investigations on cell behavior under various conditions. A review. *Cancer Res.*, 12: 847–860.

LEUCHTENBERGER, C. 1950. A cytochemical study of pycnotic nuclear degeneration. *Chromosoma*, 3: 449–473.

——, and F. SCHRADER. 1951. Relationship between nuclear volumes, amount of intranuclear proteins and desoxyribosenucleic acid (DNA) in various rat cells. *Biol. Bull., Woods Hole*, 101: 95–98.

LEWIS, E. B. 1950. The phenomenon of position effect. *Advanc. Genet.*, 3: 73–115.

LEWIS, M. R. 1923. Reversible gelation in living cells. *Johns Hopk. Hosp. Bull.*, 34: 373–379.

——. 1934. Reversible solation of the mitotic spindle of living chick embryo cells studied *in vivo*. *Arch. exp. Zellforsch.*, 16: 159–167.

LEWIS, W. H. 1947. Interphase (resting) nuclei, chromosomal vesicles and amitosis. *Anat. Rec.*, 97: 433–445.

LILLIE, R. S. 1926. The activation of starfish eggs by acids. *J. gen. Physiol.*, 8: 339–367.

——. 1931. Influence of cyanide and lack of oxygen on the activation of starfish eggs by acid, heat, and hypertonic sea water. *Biol. Bull., Woods Hole*, 60: 288–308.

——. 1941. Further experiments on artificial parthenogenesis in starfish eggs, with a review. *Physiol. Zool.*, 14: 239–267.

LIMPEROS, G. 1951. Roentgen irradiation of desoxyribonucleic acid. III. The relation of dose to degree of depolymerization *in vivo* and the influence of oxygen tension. *Cancer Res.*, 11: 325–329.

LIQUIER-MILWARD, J. 1953. Electron microscopy of thymonucleic acid. *Biochem. biophys. Acta*, 10: 5–10.

LOEB, J. 1913. *Artificial Parthenogenesis and Fertilization*. 312 pp. Univ. Chicago Press, Chicago.

LOEB, L., and K. C. BLANCHARD. 1922. The effect of various salts on the outgrowth from experimental amoebocyte tissue near the isoelectric point and with the addition of acid or alkali. *Amer. J. Physiol.*, 60: 277–307.

LOEWY, A. G. 1949. The theory of protoplasmic streaming. *Proc. Amer. phil. Soc.*, 93: 326–329.

LWOFF, A. 1951. Introduction to the biochemistry of protozoa. In *Biochemistry and Physiology of Protozoa*, Vol. I (A. Lwoff, ed.), pp. 1–26. Academic Press, New York.

MAZIA, D. 1941. Enzyme studies on chromosomes. *Cold Spr. Harb. Symp. quant. Biol.*, 9: 40–46.

——. 1954. Particulate organization of the chromosome. *Proc. nat. Acad. Sci. Wash.*, 40: 521–527.

——, and L. JAEGER. 1939. Nuclease action, protease action and histochemical tests on salivary gland chromosomes of Drosophila. *Proc. nat. Acad. Sci. Wash.*, 25: 456–461.

MCCLINTOCK, B. 1950. The origin and behavior of mutable loci in maize. *Proc. nat. Acad. Sci., Wash.*, 36: 344–355.

MCDONOUGH, E. S., M. ROWAN, and N. MOHN. 1952. Structure and staining reactions of Drosophila salivary gland chromosomes. *J. Hered.*, 43: 3–6.

MADISON, K. M. 1953. The organism and its origin. *Evolution*, 7: 211–227.

MANTON, I. 1950. The spiral structure of chromosomes. *Biol. Rev.*, 25: 486–508.

MARSHAK, A., and A. C. WALKER. 1945. Effect of liver fractions on mitosis in regenerating liver. *Amer. J. Phys.*, 143: 226–234.

MARSLAND, D. 1951. The action of hydrostatic pressure on cell division. *Ann. N. Y. Acad. Sci.*, 51: 1327–1335.

MAYER, M. E., and A. E. GRECO. 1949. The hydrolysis of nucleoproteins by cathepsins from calf thymus. *J. biol. Chem.*, 181: 853–860.

——, and ——. 1949. The nuclease activities of cathepsin preparations from calf spleen and thymus. *J. biol. Chem.*, 181: 861–870.

——, and ——. 1950. The hydrolysis of protamines by cathepsins. *Arch. Biochem.*, 29: 424–431.

MEYER, K. H., and H. MARK. 1951. Biological significance of folding and unfolding of protein molecules. *Nature, Lond.*, 167: 736.

MIESCHER, F. 1897. Die histochemischen und physiologischen Arbeiten. F. C. W. Vogel., Leipzig.

MILLER, C. O., F. SKOOG, M. H. VON SALTZA, and F. M. STRONG. 1955a. Kinetin, a cell division factor from deoxyribonucleic acid. *J. Am. Chem. Soc.*, 77: 1392.

——, ——, F. S. OKUMURA, M. H. VON SALTZA, and F. M. STRONG. 1955b. Structure and synthesis of kinetin. *J. Am. Chem. Soc.*, 77: 2662–2663.

MILLER, S. L. 1953. A production of amino acids under possible primitive earth conditions. *Science*, 117: 528–529.

——. 1955. Production of some organic compounds under possible primitive earth conditions. *J. Am. Chem. Soc.*, 77: 2351–2361.

MINSHALL, W. H., and G. W. SCARTH. 1952. Effect of growth in acid media on the morphology, hydrogen-ion concentration, viscosity, and permeability of water hyacinth and frogbit root cells. *Can. J. Bot.*, 30: 188–208.

MIRSKY, A. E. 1951. Some chemical aspects of the cell nucleus. In *Genetics in the 20th Century* (L. C. Dunn, ed.), pp. 127–154. Macmillan Co., New York.

——, and A. W. POLLISTER. 1946. Chromosin, a desoxyribose nucleoprotein complex of the cell nucleus. *J. gen. Physiol.*, 30: 117–148.

——, and H. RIS. 1947a. Isolated chromosomes. *J. gen. Physiol.*, 31: 1–6.

——, and ——. 1947b. The chemical composition of isolated chromosomes. *J. gen. Physiol.*, 31: 7–18.

——, and ——. 1950. The composition and structure of isolated chromosomes. *J. gen. Physiol.*, 34: 475–492.

MIYAJI, T. 1952. Some observations on the volume of the nucleus of spontaneous hepatomas in mice. *J. nat. Cancer Inst.*, 13: 627–645.

MORGAN, T. H. 1927. *Experimental Embryology.* 766 pp. Columbia Univ. Press, New York.

MULLER, H. J. 1947. The gene. *Proc. Roy. Soc. Lond.*, B, 134: 1–37.

NEURATH, H. 1939. The apparent shape of protein molecules. *J. Am. Chem. Soc.*, 61: 1841–1844.

OHLMEYER, P. 1950. Experimentelle Bindung von Eiweisskörpern an Zellkerne und Nukleinsäuren. *Biochim. biophys. Acta.* 4: 229–231.

——, H. BRILMAYER, H. KRUPP, U. OLPP, and L. D. MEHMKE. 1949. Experiments in binding of proteins with nuclei and nucleic acids. *Z. Naturf.*, 4b: 263–269.

OPARIN, A. I. 1938. *The Origin of Life.* 270 pp. Translated by S. Morgulis. Macmillan, New York.

PALAY, S. L., and A. CLAUDE. 1949. An electron microscope study of salivary gland chromosomes by the replica method. *J. exp. Med.*, 89: 431–438.

PAULING, L. 1953. Aggregation of globular proteins. *Disc. Faraday Soc.*, 13: 170–176.

——, and R. B. COREY. 1953. A proposed structure for the nucleic acids. *Proc. nat. Acad. Sci., Wash.*, 39: 84–97.

PEDERSON, K. O. 1938. Ultracentrifugal studies on protein mixtures. *C. R. Lab. Carlsberg, sér chim.*, 22: 427–433.

PETERMANN, M. L., and C. M. LAMB. 1948. The nucleohistone of beef spleen. *J. biol. Chem.*, 176: 685–693.

POLLISTER, A. W. 1952. Nucleoproteins of the nucleus. In *The Chemistry and Physiology of the Nucleus. Expt. cell Res.*, Suppl. 2: 59–70.

——, H. SWIFT, and M. ALFERT. 1951. Studies on the desoxypentose nucleic acid content of animal nuclei. *J. cell. comp. Physiol.*, 38, Suppl. 1: 101–119.

——, and A. E. MIRSKY. 1946. The nucleoprotamine of trout sperm. *J. gen. Physiol.*, 30: 101–116.

POTTER, V. R., R. O. RECKNAGEL, and R. B. HURLBERT. 1951. Intracellular enzyme distribution; interpretations and significance. *Fed. Proc.*, 10: 646–653.

PROKOFYEVA-BELGOVSKAYA, A. A. 1948. Heterochromatization as a change of chromosome cycle. *J. Genet.*, 48: 80–98.

RASHEVSKY, N. 1938. *Mathematical Biophysics. Physico-Mathematical Foundation of Biology.* 669 pp. Univ. Chicago Press, Chicago.

——. 1939. The mechanism of cell division. *Bull. math. Biophys.*, 1: 23–30.

——. 1941a. Some remarks on the movement of chromosomes during cell division. *Bull. math. Biophys.*, 3: 1–3.

——. 1941b. The dynamics of cell constriction during division. *Bull. math. Biophys.*, 3: 57–62.

——. 1948. Can elastic stresses in gels cause the elongation and division of a cell? *Bull. math. Biophys.*, 10: 85–89.

——. 1952. Some suggestions for a new theory of cell division. *Bull. math. Biophys.*, 14: 293–305.

REICHMANN, M. E., B. H. BUNCE, and P. DOTY. 1953. The changes induced in sodium desoxyribonucleate by dilute acid. *J. Polym. Sci.*, 10: 109–119.

——, R. VARIN, and P. DOTY. 1952. The molecular weight and shape of desoxypentose nucleic acid. *J. Am. chem. Soc.*, 74: 3203–3204.

RICHARDS, A. 1917. The history of the chromosomal vesicles in Fundulus and the theory of genetic continuity of chromosomes. *Biol. Bull., Woods Hole*, 32: 249–291.

RILEY, D. P., and U. W. ARNDT. 1953. X-ray scattering evidence regarding the protein-nucleic

acid combination in nucleoproteins. *Nature, Lond.*, 172: 294–295.

RIS, H., and A. E. MIRSKY. 1949a. Quantitative cytochemical determination of desoxyribonucleic acid with the Feulgen nucleal reaction. *J. gen. Physiol.*, 33: 125–146.

——, and ——. 1949b. The state of the chromosomes in the interphase nucleus. *J. gen. Physiol.*, 32: 489–502.

ROBERTS, H. S., and N. G. ANDERSON. 1951. Studies on isolated cell components. III. A cytological study of the effects of heparin on isolated nuclei. *Exp. Cell Res.*, 2: 224–234.

ROWEN, J. W. 1953. Light-scattering studies of sodium desoxyribonucleate. *Biochim. biophys. Acta*, 10: 391–401.

ST. AMAND, G. S., N. G. ANDERSON, and M. E. GAULDEN. 1955. The effect of agmatine on mitosis in the neuroblasts of the grasshopper, *Chortophaga viridifasciata*. *Bull. Ass. SE Biologists*, 2: 10.

SANDERSON, J. A., and E. O. HULBURT. 1954. Sunlight as a source of radiation. In *Radiation Biology* (Alexander Hollaender, ed.) Vol. II, McGraw-Hill, New York, in press. Pp. 95–118.

SCHNEIDER, R. 1953. Nucleoprotamin. VI. Karyometrische Untersuchungen an durch "kunstliche Befruchtung" entstandenen Bachsaibling-Embryonen. *Hoppe-Seyl. Z.*, 294: 74–79.

SCHNEIDER, R. M., and M. L. PETERMANN. 1950. Nuclei from normal and leukemic mouse spleen. I. The isolation of nuclei in neutral medium. *Cancer Res.*, 10: 751–754.

SCHNEIDER, W. C., and G. H. HOGEBOOM. 1951. Cytochemical studies of mammalian tissues: The isolation of cell components by differential centrifugation: A review. *Cancer Res.*, 11: 1–22.

SCHOMER, H. A. 1936. The effects of radiation on enzymes. In *Biological Effects of Radiation* (B. M. Duggar, ed.), Vol. II, pp. 1151–1165. McGraw-Hill, New York.

SCHRADER, F. 1953. *Mitosis. The Movements of Chromosomes in Cell Division*. Second ed. 170 pp. Columbia Univ. Press, New York.

SEIFRIZ, W. 1952. The rheological properties of protoplasm. In *Deformation and Flow in Biological Systems* (A. Frey-Wyssling, ed.), pp. 3–156. Interscience Pubs., New York.

——. 1953. Mechanism of protoplasmic movement. *Nature, Lond.*, 171: 1136–1138.

SERRA, J. A. 1947. Composition of chromonemata and matrix and the role of nucleoproteins in mitosis and meiosis. *Cold Spr. Harb. Symp. quant. Biol.*, 12: 192–210.

SHAPIRO, H., and A. K. PARPART. 1937. The osmotic properties of rabbit and human leucocytes. *J. cell. comp. Physiol.*, 10: 147–163.

SHAVER, J. R. 1953. Studies on the initiation of cleavage in the frog egg. *J. exp. Zool.*, 122: 169–192.

SHINKE, N. 1937. An experimental study on the structure of living nuclei in the resting stage. *Cytologia, Tokyo*, Fujii jubilee vol., 449–463.

SHOOTER, K. V. 1954. Physical state of deoxyribonucleic acid in rat thymus homogenates. *Nature, Lond.*, 173: 824–825.

SOROF, S., and P. H. COHEN. 1951. Electrophoretic and ultracentrifugal studies on the soluble proteins of various tumors and of livers from rats fed 4-dimethylaminoazobenzene. *Cancer Res.*, 11: 376–382.

SPARROW, A. H. 1951. Radiation sensitivity of cells during mitotic and meiotic cycles with emphasis on possible cytochemical changes. *Ann. N. Y. Acad. Sci.*, 51: 1508–1540.

——, and F. M. ROSENFELD. 1946. X-ray-induced depolymerization of thymonucleohistone and of sodium thymonucleate. *Science*, 104: 245–246.

STEDMAN, E., and E. STEDMAN. 1950. Cell specificity of histones. *Nature, Lond.*, 166: 780–781.

——, and ——. 1951. The basic proteins of cell nuclei. *Phil. Trans.*, 235: 565–596.

STERN, H., and A. E. MIRSKY. 1952. The isolation of wheat germ nuclei and some aspects of their glycolytic metabolism. *J. gen. Physiol.*, 36: 181–200.

——, and ——. 1953. Soluble enzymes of nuclei isolated in sucrose and non-aqueous media. *J. gen. Physiol.*, 37: 177–187.

STERN, K. G. 1949. Experiments on the size and shape of chromosomal nucleoproteins and their bearing on gene structure. *Exp. Cell Res.*, Suppl. 1: 97–99.

——. 1952. Problems in nuclear chemistry and biology. *Exp. Cell Res.*, Suppl. 2: 1–12.

——, and S. Davis. 1946. Studies on thymus nucleohistone. *Fed. Proc.*, 5: 156–157.

STEVENS, C. E., R. DAOUST, and C. P. LEBLOND. 1953. Rate of synthesis of desoxyribonucleic acid and mitotic rate in liver and intestine. *J. biol. Chem.*, 202: 177–186.

STRUGGER, S. 1930. Beitrag zur Kolloidchemie des pflanzlichen Ruhekernes. *Protoplasma*, 10: 363–378.

SVEDBERG, T., and S. BROHULT. 1938. Splitting of the haemocyanin molecule by ultraviolet light. *Nature, Lond.*, 142: 830–831.

SWIFT, H. 1953. Quantitative aspects of nuclear nucleoproteins. *Int. Rev. Cytol.*, 2: 1–76.

TAYLOR, B., J. P. GREENSTEIN, and A. HOLLAENDER. 1948. Effects of X-radiation on sodium thymus nucleate. *Arch. Biochem.*, 16: 19–31.

TYLER, A. 1941. Artificial parthenogenesis. *Biol. Rev.*, 16: 291–336.

VAN NIEL, C. B. 1949. The comparative biochemistry of photosynthesis. In *Photosynthesis*

in Plants (J. Franck and W. E. Loomis, ed.), pp. 437–495. Iowa State Coll. Press, Ames.

VENDRELY, R., and C. VENDRELY. 1948. La teneur du noyau cellulaire en acide désoxyribonucléique à travers les organes, les individus et les espèces animales. *Experientia*, 4: 434–436.

——, and ——. 1949. La teneur du noyau cellulaire en acide désoxyribonucléique à travers les organes, les individus et les espèces animales. *Experientia*, 5: 327–329.

——, and ——. 1953. Arginine and deoxyribonucleic acid content of erythrocyte nuclei and sperms of some species of fishes. *Nature, Lond.*, 172: 30.

UREY, H. C. 1952. *The Planets*. 245 pp. Yale Univ. Press, New Haven.

WATSON, J. D., and F. H. C. CRICK. 1953. Molecular structure of nucleic acids; a structure for deoxyribose nucleic acid. *Nature, Lond.*, 171: 737–738.

WEIMAR, V. L. 1953. Calcium binding in frog muscle brei. *Physiol. Zool.*, 26: 231–242.

WILBUR, K. M., and N. G. ANDERSON. 1951. Studies on isolated cell components. I. Nuclear isolation by differential centrifugation. *Exp. Cell Res.*, 2: 47–57.

——, ——, and M. V. SKEEN. 1949. Isolation and properties of rat liver nuclei. *Anat. Rec.*, 105: 486.

WILKINS, M. H. F., and J. T. RANDALL. 1953. Crystallinity in sperm heads: Molecular structure of nucleoprotein in vivo. *Biochim. biophys. Acta*, 10: 192.

——, A. R. STOKES, and H. R. WILSON. 1953. Molecular structure of deoxypentose nucleic acids. *Nature, Lond.*, 171: 738–740.

WILSON, J. W., and E. H. LEDUC. 1947. Mitotic rate in mouse liver following intraperitoneal injection of liver, kidney and egg yolk. *Anat. Rec.*, 97: 471–494.

——, and ——. 1950. Abnormal mitosis in mouse liver. *Amer. J. Anat.*, 86: 51–74.

WOODGER, J. H. 1948. Observations on the present state of embryology. *Symp. Soc. exp. Biol.*, 2: 351–365.

YASUZUMI, G., Z. ODATE, and Y. OTA. 1951. The fine structure of salivary chromosomes. *Cytologia, Tokyo*, 16: 233–242.

ZAKRZEWSKI, Z. 1932. Die Rolle des Prothrombins und Heparins bei der Proliferation und Differenzierung von Geweben. Untersuchungen in Vitro. *Arch exp. Zellforsch.*, 13: 152–175.

ZAMENHOF, S., H. E. ALEXANDER, and G. LEIDY. 1953. Studies on the chemistry of the transforming activity. I. Resistance to physical and chemical agents. *J. exp. Med.*, 98: 373–397.

ZEIGER, K. 1935. Zum Problem der vitalen Struktur des Zellkernes. *Z. Zellforsch.*, 22: 607–632.

ZOLLINGER, H. U. 1948. Cytologic studies with the phase microscope. III. Alterations in the nuclei of "resting" and dividing cells induced by means of fixatives, anisotonic solutions, acids and alkali. *Amer. J. Path.*, 24: 797–811.

PERCEPTION OF PATHWAYS BY FISHES IN MIGRATION*

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IN ORIENTATION a fish is visually more handicapped than a bird or a land animal because light is absorbed rapidly by water, hence limiting vision in deeper water. In addition, clear vision in water is often poor owing to turbidity. On the other hand, the human observer who attempts to determine how the fish find their way about is also handicapped because not only is his own vision limited but most of his information is gained through indirect observations.

It is known that salmon and eels make long journeys from their place of birth. How do they find their way? In attempting to contribute to an answer to this question I shall at the outset assume that a fish, in swimming to a feeding or breeding area, does so by orienting to physical, chemical, or biological stimuli in the environment. The specifications shall be that orientation must have a physiological basis and cannot be explained in the realm of clairvoyance, or extrasensory perception.

Reviews (Scheer, 1939; Shapovalov, 1941; Scheuring, 1930) of recent years on migration in fishes cite evidence from numerous investigations establishing that most species of salmon return to a home stream to spawn. Moreover, it is established that the eel (Schmidt, 1906) migrates from the United States and Europe to spawn in the Sargasso Sea and its young return to their respective continents! This review assumes the home stream behavior in salmon and the return of the eel to the Sargasso Sea to be established behavior patterns, and that to explain the so-called homing theory is not a matter of establishing that it exists, but of trying to explain how the fish get home.

That the majority of silver, sockeye, and king salmon, for instance, return to their natal stream is a phenomenon which challenges the biologist for an explanation. That some go astray must be expected as an aspect of biological variation, a firmly established characteristic of living things. This review, therefore, will not recount the evidence for directive orientation, but will search out whatever knowledge will help to interpret how the fish accomplishes these feats and to point up what lines of research might be productive in uncovering the secret they have kept hidden from us so long.

Because the subject of the migration of fishes is so large, were all species to be reviewed, I will stress here the phases of orientation which apply to the salmon and eel, although in passing other fishes will be mentioned.

For the purpose of appraising the various senses and their role in orientation during migration, I shall treat each sensory system separately.

VISUAL POINTS OF REFERENCE

Owing to the angle of diffraction of water, the actual visual field of a fish is smaller than for a land animal. Moreover, the deeper it goes, the less it is able to view an object on the shore (Walls, 1941). The sun, for example, would be seen well when it is fairly high in the heavens, and therefore its light would be only a diffuse beacon at early and late periods of the day, and in winter (northern hemisphere) throughout the entire day. However, if the sun were below the visual angle it might be expected that there would be, in clear water, a greater intensity of light in the direction of the sun. The deeper one goes, the more the light appears to come predominantly from overhead; nevertheless Whitney (1941) gives evidence that at one point in the Atlantic Ocean there was a directional component as deep as 40 meters when measured by a rotatable photocell. A fish could possibly detect a rough compass direction from which the rays of the sun are coming. A comparable situation is observed by man: before sunrise a glow in the east

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definitely marks this segment of the heavens, even though the sun is not seen.

It is known that other animals use the sun in near orientation (birds: Kramer, 1952, 1955; bees: von Frisch, 1951) and have the additional facility of maintaining their goal (feeding site) constant by using the sun as a point of reference, and correcting continuously for its movement during the day. They have therefore a biological chronometer and a sun compass. Such a mechanism, however, has not been demonstrated for fish and should be looked into seriously.

While the water is a poor visual medium, it must be kept in mind that great quantities of light are not required for a visual stimulus. Merely a single quantum of light falling on a cone, or on a rod of the eye of man will induce a stimulus (Hecht, Schlaer, and Pirenne, 1942). The amount of light required for this stimulus, if measured at the cornea, might be of the order of 50 quanta, but even this is a very small quantity of light. Also recent studies of Leibowitz, Meyers, and Grant (1955) show that man can localize an object in the visual field with an accuracy which is independent of the magnitude of the primary light source. These observations furnish circumstantial proof that the strength of light may not be the all-limiting problem in under-water orientation, provided the fish migrate in the surface waters where there is light—starlight not excepted. Määr (1947) gives good evidence that adult eels migrate near the surface at night. It is also pertinent here that Scheuring (1930), quoting Grassi and Calandruccio (1897), called attention to the fact that the eel's eye prior to migration undergoes extreme enlargement (Fig. 1). Recent studies of the distribution of another significant homing fish, the salmon, demonstrate that it occurs over 1000 miles from the shore and is captured at sea with gill nets set near the surface, according to reports of the U. S. Fish & Wildlife Service (Sportfishing Review, 1955; Com. Fish. Review, 1955). These findings point up the need for more research into the vision of fishes and the possible use of celestial reference points in open-water navigation.

It appears that elvers travel both by day and by night at sea; at night they swim at a much higher level than by day (Deelder, 1952); also on flood tide they travel at a higher level than on ebb. The implication is that at the flood tide the turbidity is higher.

Grundfest's studies (1932) of the minimal light necessary to produce a visual response in the sunfish *Lepomis* have been converted by Clarke (1936) into depths in water at which there would be enough natural light to correspond with this value. At high noon the sunfish could see at 430 m. in the Sargasso Sea; 180 m. on the Georges Bank. It can be repeated that visual cues cannot be eliminated in a consideration of orientation at sea.

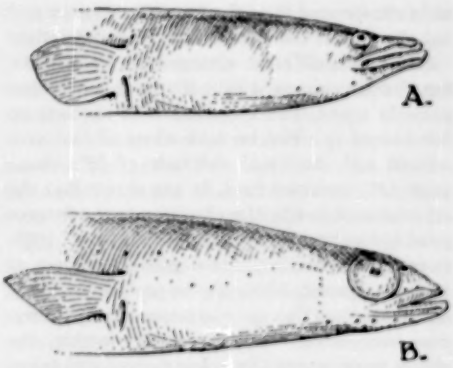

FIG. 1. ENLARGEMENT OF THE EYE OF THE EEL PRIOR TO MIGRATION
(Adapted from both Scheuring, 1930, and Schmidt, 1906)

H. T. Odum, of Duke University, has suggested to me that fish in a tropical sea, where east-west currents are the rule, could maintain a definite course by swimming at right angles to foam lines or to surface "weed" patches which line up along such wave formations. Moreover, light bars and ocean swells are physical stimuli that may be used, according to suggestions made by T. Bullock and J. Isaacs, of the University of California.

CELESTIAL MARKS FOR ORIENTATION

To make an approach to this problem I set out, in a simple experiment (Hasler, 1956; see Fig. 2), to determine if a fish could locate a food source when an elevated light, simulating a sun in a fixed position, was its principal point of reference.

In an experimental system in which the objective was to determine if the minnow *Phoxinus* could orient itself in a round tank to a feeding station at 0° when a "celestial mark," a lamp spot at 45° in the "heavens" (altitude of 57°; visual angle 66°), was in competition with environmental features, it was demonstrated that the latter were more important. This was indeed surprising, because the experimental tank was of uniformly appearing metal. Fine solder marks and irregular oxidation patterns on the wall and bottom were demonstrated to have been the foci which assisted the fish to learn that reward was

to be experienced from the "north" container and not at a similar container in the "south" position.

In using a different arrangement to test the fishes' ability to use a light source as a reference point in orientation, I conducted blank tests on fish trained in a circular tank where all foci were rotated and the "sun" (altitude of 52°; visual angle 62°) remained fixed. It was shown that the celestial mark (artificial sun) was used as a reference point in locating a feeding container at a 90° angle from it (0°). The opposite negative container at 180° was ignored. Although the problem of recognizing the "sun" as an orientation point of reference was learned only after long training, the ability to do so must be acknowledged and taken into consideration in an explanation of the migration-orientation of fishes.

True, the immediate environmental marks were most readily used in orientation in this small, circular tank, a fact which emphasizes and verifies the remarkably keen vision of this species. Indeed, it prescribes to them unusual abilities heretofore surmised but not supported with quantitative data. It is apparent, therefore, that like the bee (von Frisch and Lindauer, 1954) the fish finds landmarks a distinct aid to orientation when they are in competition with the sun, but the degree to which the sun influences the fish's direction-finding must still be worked out.

In tests on pond fishes (unpub.), we have found that displaced green sunfish (*Lepomis cyanellus*), which returned to their territory unerringly, were disoriented when placed in an adjacent unfamiliar pond.

Also, in our studies, marked largemouth bass (*Micropterus salmoides*) in round lakes, if displaced, were found to return to their territory more accurately than those in an irregular lake. Homing in large and small mouth bass has been reported by Cooper (1953) Larimore (1952), and Shoemaker (1952). Aronson (1951) found evidence that a gobiid fish learns the contours of the ponds during high tides and jumps directionally over the sand towards its home pool at low tide when the ponds are separated by small strips of land. Aronson refers to early work along this line as follows:

> Goldsmith (1905, 1912, 1914) has demonstrated clearly the existence of a topographic memory and its dominance over the memory of form and color. This is mostly a visual response, but a motor component (memory of movement already effected) is not excluded. This dominance of topographic memory is manifested, by its definiteness when size, form and color are in conflict. Moreover, memory of a site was found to be more enduring than of color or form.

Following the sun navigation concept further, it must be admitted that a fish in clear water and near the surface might readily use the sun in orientation. We know, for example, that the perch in Lake Mendota, Wisconsin, make migrations to shore at sundown (Hasler and Villemonte, 1953). Here the setting sun might be a stimulus to initiate migration, but it could also be a reference point, if the fish were not too deep, provided a second directional component were discernible. The implication is clear that the sun could play a role at least in near orientation in some fishes swimming in relatively shallow water.

I wish to emphasize that my evidence of the ability of fishes to recognize a celestial light source does not prove that the fish can take into consideration the daily movement of the sun or a star. Further tests must be carried out to determine if the fish possesses an "internal chronometer" useful in establishing its course by use of the sun as do birds and insects. My data are suggestive only, because a fixed light source is, in the last analysis, just another type of object. Since in my initial study the artificial sun did not move in an arc, it may have presented the fish with a confusing signal, and that may explain why it was so difficult for them to learn to use the fixed "sun" in orientation.

Should this be demonstrated for fish there remains a question about how it could be used in navigation over long distances, as is still unproved for birds (Kramer, 1955). Apparently other sensory and analytical equipment is necessary for this feat, because as it seems now the physiological clock and "compass" are aids principally for local direction-finding.

TACTILE AND AUDITORY REFERENCES

Deelder (1952) states:

> With regard to elvers, let us suppose with Verwey (1949) that they have an eastward sense of direction. Elvers swimming in this direction after metamorphosis will sooner or later reach a coastline (European). Now it has been proved (see also Diesselhorst, 1938) that eels can hear. On an oceanic coast such as the Atlantic coast of Europe, there will be a surf, the beat of which we may assume elvers can hear, the more so because water transmits sound much better than air. Just as a man can move along the shore with his eyes closed,

orientating himself with his ears towards the breakers, so may elvers be able to do it.

In this connection Westenberg (1952) states:

> Certain Indonesian fish are able to swim parallel to a coast; they are even able to keep along a certain depth contour . . . owing to the ruffled water surface sending sound vibrations downward which are reflected from the bottom. This will set up a resonance with an average wave-length of four times the depth, so that a particular resonance frequency will correspond to a certain depth.

In this regard, is it possible that sockeye salmon can "hear" the noise of the outlet of a lake and orient to it from some distance when they begin the downstream migration?

In support of the view that fish may have the ability to locate sounds, Kleerekoper and Chagnon (1954) have furnished evidence that trained fish (*Semotilus atromaculatus*) were able to locate the source of a vibration to which they had been conditioned, in an experimental tank (47 x 42 x 35 inches) in response to vibrations from two sources and at two different intensities but at the same frequency (50 c.p.s.). Measurements of the magnitude of sound in the tank indicated that the intensity gradients existed along the pathways followed by the fish.

An original suggestion relevant to the above problems stems from the suggestion of Andriascheff (1944) that seismic vibrations may direct the eel. Määr (1947) commented on this as follows: "If one takes into consideration that the waves of the Atlantic against the European continent are perceived at the seismological station at the University of Tartu (formerly Estonia), is it not possible, that the migration path of the migrating eel could be guided by perception of seismic vibrations?"

Deelder (1952) analyzed the rate of positive transport of elvers in the North Sea by tides, on the assumption that the elvers could select the most advantageous ebb and flood during night and day and on either surface or bottom. He arrived at a value of 6.5 km. per day, but they must make 20 km. per day to explain the observed difference in initial arrival time between Land's End, England, and Denmark. They then must swim vigorously and be fairly well oriented. This implies that they can recognize ebb and flood. He comments: "On the ebb they swim against the stream and on flood with it. They might do this on the bottom during the day, but how could they do this in the upper waters?"

Deelder ascribes to the eel a "sense of direction." He adds: "The difference in turbulence enables the elvers to distinguish between ebb and flood flows when they are on the bottom [he states however that he found no support for this idea in his study] and that they are able to 'recollect' these directions when in the upper water layers."

This "sense of direction" concept does not help to explain the fact, because the sense must be stimulated by some tangible force. We are no farther along with this concept than with the term "instinct for migration." Deelder himself appeared to be aware of this weakness in his theory, for he added other possible explanations: "They may keep to a direction with the help of the electric currents generated by the movements of sea water. The horizontal component of the current is perpendicular to the flow of the sea water. If elvers are able to perceive very small currents, they can align themselves with the water flow by taking up a position in which no electrical current runs from snout to tail or the reverse. Dr. Groen has estimated that in elvers this current would be almost 1×10^{-10} amp./mm.^{2} for a water speed of 1 m./sec. provided that the electrical resistance of elvers can be perceived, but Uzuka (1934) found that a catfish could perceive a current of 1×10^{-7} amp. which is 1000 times greater than the value mentioned above." He poses the question:

"What are the consequences of these orientation hypotheses?" "Elvers travel in the same line as the tidal streams where these are present. . . . Evidently they reach the southern North Sea . . . as the flood stream is north-going . . . and migrate southward with the southgoing flood stream."

John (unpub.) observed that blinded *Electris pisonis* exhibit a high sensitivity to slight disturbances in the water, avoid collisions with solid surfaces in their path, and navigate very well in the absence of visual cues. He has written further: "Limited observations indicate, as has been suggested in the literature [see his cited literature] that fishes deprived of visual cues are able to avoid collisions with objects through their detection of an increase in the water pressure that develops as they approach a solid surface. The literature indicates that fish detect such increase in pressure through their neuromasts, and end organs of their sensory lines and canals."

He has also given evidence that his *Anoplichthys* and blinded *Astyanax* collided with solid surfaces if they depended on their memory of spatial relationships rather than on their perception of mechanical cues, and showed, also, that this fish never succeeded in avoiding pressure-transparent objects.

What appears to be another appropriate site and species to investigate for purposes of sorting out the hydrographic or celestial factors which guide a pelagic species in open water is suggested by the recent work of Nümann (1955) on the Atlantic bonito (*Sarda sarda*). Marked specimens from the Black Sea were reported to have moved with surprising speed through the Bosporus and the Sea of Marmara into the Aegean Sea, beginning their migration in late summer, and at times of fair weather. Nümann suspected that the currents are the guiding stimuli. I hope someone can continue his studies, for I understand he has moved recently to work on the Lake of Constance (der Bodensee).

OLFACTORY ORIENTATION

Our own investigations of odor perception in fishes (see Hasler, 1954) point up the likelihood of odor as the directive guidepost to homing salmon upon reaching their home river.

That salmon return, in the great majority of cases, to spawn in the stream or tributary in which they were reared, is acknowledged as fact by most modern fisheries biologists. Although previous workers who have investigated this phenomenon have advanced the idea that chemical stimuli may influence the movements of salmon, no one has been able to guide salmon to stream artificially.

It has been postulated by Hasler and Wisby (1951) that there is, in river and creek water, some characteristic odor to which young salmon become conditioned while in the stream, and which they recognize and to which they orient upon reaching the parent stream as mature migrants. This theory embodies the principle that a salmon returning to its parent stream reacts differently to the odor of that stream than to that of any other. In order for a salmon to return to its home stream there must be some possibility of a differential reaction, not a simple response to a repellent or an attractant. This guiding odor must remain constant from year to year and have meaning only for those salmon which were conditioned to it during their fresh-water sojourn.

This theory presents three distinct problems:

(1) Do streams have characteristic odors to which fish can react? If so, what is the nature of the odor?

(2) Can salmon detect and discriminate between such odors if they do exist?

(3) Can salmon retain odor impressions from youth to maturity?

In order to answer the first question, a group of bluntnose minnows, fish of proven olfactory acuity, were trained to discriminate between the chemical differences of two Wisconsin creeks. That scent-perceiving organs were the sole means of discrimination in these tests was proven by destroying the olfactory tissue of trained fishes, after which they no longer responded to the training odors. Chemical analysis of the stream waters indicated that the major difference between them was in the total organic nitrogen fraction. Experimental evidence to substantiate this was obtained by separating the water into various fractions and then presenting these to trained fishes. The fish trained previously to natural water did not react to the inorganic ash, or to the distillate or residue of water fractionated at 100°C. However, they recognized the distillate, but not the residue, of water fractionated by vacuum distillation at 25°C.—a strong indication that the odorous stimulant is a volatile substance.

A test was conducted of the retentive capacities of the trained minnow, and it was determined that even this fish, which is not specialized in this respect, could differentiate between the odors for a comparatively long period after cessation of training. Learned behavior was found to be retained longer by young fish than by old ones.

The method of training which had been used with such success with the minnows was then applied to salmon fry. After a short period of training it was evident that these fish too could discriminate between the odors of the two Wisconsin creeks.

Hasler and Wisby (1951) proposed to employ an artificial substance to which salmon fry could be conditioned and which could then be used to decoy them, upon their return, into rehabilitated streams, formerly dammed or polluted, or to salvage a run which would not be able to pass a newly constructed power dam. Such an odor must be neither a repellent nor an attractant for the unconditioned salmon.

Wisby (Univ. Wis. Thesis, 1952, unpub.) de-

signed an apparatus to test the reactions of unconditioned salmon to various organic odors which might be used for the above purpose. This unit consists of four arms which converge on an enlarged central compartment. Water is introduced into the upper end of each arm and cascades down a series of eight small falls until it enters the center compartment, from which it exits through a drain. The entrance to each of the four arms is guarded by a gate, and all of the gates can be raised by pulling a single cord.

Salmon fry were placed in the center compartment and, upon introduction of an odor into one of the arms, the gates were raised to permit the fish to enter the arm. Their distribution after the test was then noted and compared with the distribution obtained when no odor was present.

Many organic odors were presented to unconditioned salmon, and their reactions noted. Of these, none was found which would attract salmon, many seemed not to be perceived, and the remainder were distinctly repellent in action at the concentrations used. Of the latter, only two were deemed suitable for further testing. One of these, dicyclopentadiene, proved to be so insoluble as to render accurate dilutions impossible.

It was observed that these fishes were not totally repelled by dilute solutions of morpholine, although it could easily be detected in concentrations as low as 1×10^{-6} p.p.m. Although the minimum detectable concentrations were not established, the concentrations presented indicate a sensitivity to chemical stimulation far exceeding that reported for any fish tested previously.

It appears, then, that the compound morpholine fits the requirements mentioned previously. It is soluble in water, thus permitting accurate dilutions; it is detected in extremely low concentrations, thus making the treatment of large volumes of water feasible; and it is chemically stable under stream conditions. Furthermore, at these low concentrations, it is neither an attractant nor a repellent for unconditioned salmon, and thus should have meaning only for those salmon previously conditioned to it. Field tests should be conducted to determine whether salmon fry and fingerlings which have been conditioned to morpholine can be decoyed to a stream other than that of their birth, upon their return to fresh water as mature migrants. An experiment of this kind to determine the nature of imprinting is of the highest importance relative to our hypothesis.

Matthews (1955) has made a digest of the comments of Mr. T. A. Stuart on the homing of trout to tributaries of a Scottish lake (Brown Trout Research Laboratory, Pitlochry, Scotland):

> The trout has a strong homing tendency and, of many hundreds marked, none has afterwards been recovered in a stream other than that in which it was originally captured, except when the latter has been blocked. From 1952 the fry has been marked in this way, so that it is definitely known that the individual was born in a particular stream. Again strong homing tendencies have been demonstrated. Experiments have been made in which ripe fish moving up a stream are removed and released in streams on the opposite side of a large reservoir into which the streams emptied, a distance of more than a mile. No fish was recaptured in the stream to which it had been transferred; but about half those released were recovered and all save two were back in the original stream from which they had been removed. The successful homers did not only have to detect the mouth of the home stream once they were in the reservoir, but also actively to leave the foreign stream, swimming downstream against the mass of incoming fish for whom that particular stream was home. Mr. Stuart could not offer any explanation for the way in which the fish could re-orientate themselves in this manner. He thought it unlikely to be based on the detection of chemical factors, a view he maintained in the subsequent discussion when the work of Hasler was mentioned. This latter worker has claimed that fish can 'smell' the difference between streams from the difference in their organic contents.

I have suggested to Mr. Stuart that he test this hypothesis by collecting water from two of these streamlets to determine if these trout, in the laboratory, can be trained to discriminate them by odor.

Pursuing further this concept of the recognition by odor of a home stream, Wisby and Hasler (1954) captured sexually ripe coho salmon at two branches of the Issaquah River in Washington and returned them downstream below the fork to make the run and selection of stream again. In half of them the nasal sac was plugged with cotton. The great majority of normal fish selected again the stream of first choice, while the plugged-nose fish returned in nearly random fashion. No comparable pressure trauma was applied to the control fish; nevertheless, this experiment is indicative of the important role that the functional olfactory system has in orientation.

That guide posts other than odor are influencing the movements of salmon at sea is shown by the

observations of Shapavolav and Taft (1954), who cited data to prove how in some cases the home river could not possibly have any influence on the activities of the salmon near the mouth of a home river because in some creeks in California the mouths of the creeks are closed by sand bars during the summer so that no freshwater can enter the ocean.

Huntsman (1939) postulated on the basis of modest data that freshets induce Atlantic salmon to run in the Margaree River (Canada). Hayes (1953) confirmed this observation with considerably more data, but pointed out how wind and tide might reduce the effect of freshets. The major runs can occur without the aid of natural or artificial freshets and can be maintained by a steady flow of water during the run season. He postulates that the effect is due to a diluting of the salt in the estuary or the direct effect of the current. In the light of our studies may I suggest that it could be odors from the organic material in the freshets.

Fontaine and Vibert (1952) believe salinity-gradients to be of value in the location of a home stream by salmon. Discrimination of chemical differences by fishes has been well established, but no one has demonstrated an ability of fishes to follow gradients. Moreover, the sensory physiology of salt-detection is in need of careful analysis.

Collins (1952) has revived the notions of Powers (1943) concerning CO_2 tensions by a series of experiments demonstrating the repelling actions of CO_2 on the alewife *Pomolobus pseudoharengus*. This explanation of homing in anadromous fishes suffers from the same weakness expressed above. If fishes were attracted or repelled by substances such as CO_2, that does not signify that they are responding to it in homing. Indeed, it would seem to preclude the possibility. If this were the case salmon might be expected to follow a gradient regardless of their origin.

A home-stream behavior for the shad *Alosa sapidissima* appears now to have been established by Talbot (1956, and unpub.). Whether this species' streamward journey is influenced by odors will be interesting to study.

Odor could be an initiating factor in the seaward migration of the silver eel. Lowe (1952) has observed that most eels migrate when rains coincide with moonless periods. Few eels ran when there was a full moon; the run could be checked experimentally by artificial light. She concluded that the rains or some associated factor, possibly water temperature, acts as a trigger stimulus starting downstream migration. Personally, I cannot rule out the possibility that the increased rains could bring in a greater concentration of odorous material from the watershed which would reach greater than threshold values to a migration-sensitized eel.

Several reviewers have quoted Schäffer (1919) on the migration of eels on land. These are very interesting experiments conducted apparently by a hobbiest. It is surprising that others have not followed up on these tests. He suggests that the "smell of the sea" may be an orienting factor. Since this reference is not easily available in the original I will abstract it here rather fully.

Schäffer (1919) trapped eels in 1908 about 50 km. from Stockholm (southern part of the "Stockholmer Schären") and 18 km. from the entrances of the Baltic Sea. He noted in his account that:

A human can smell the sea on a light wind from a distance of several kilometers, "wieviel mehr wohl ein Wassertier wie der Aal."

Eels cannot make much headway if the ground is dry—because they lose too much mucus.

Exp. 1, July 1908. Light wind NNW. Temp. 16.7°C. Barometer 766.5 mm. Hg. Clear.

Seven eels caught on hook and line were transported in a bucket of water—20 min. landward behind a hill—the meadow was sprayed with water in a 10 m. circle and the eels were released with heads toward the east. They immediately reversed themselves to migrate westward in the direction of the bay and moved straight on for 200 m.

Exp. 4, July 1908. Wind slight NNW. Rain. Temperature 7.6°C. Barometer 756.5 mm. Three eels carried 300 m. landward (no need to moisten the grass). They started right off toward water and reached shore in 20 min.

8 July 1908. Light wind NNE, fair. Temperature 10.4°C. Barometer 759.1 mm. Three small eels carried 350 m. behind a hill. Two moved around the hill toward water. One took the long way and was found the next day dried up.

7 July. Three more carried 2 km. over a hill. They moved toward nearest water that lay nearer the point I carried them from.

28 July. Six eels—400 m. Grass wet—they moved fast. They moved toward water. Two were lost.

Five other tests verified the above observations.

25 Sept. 1908. NE wind, thick fog. Temperature

6.9°C. Barometer 768.2 mm. Three eels 4 km. landward. They took off not toward the sea arm 4 km. away, but toward a brook 2 km. away. One reached the brook. A slight wind could have come up from southeast.

The simplicity of these tests causes me to wonder why they have not been verified by duplication. Certainly here is a novel means of orientation which needs looking into.

HYDROGRAPHIC REFERENCE POINTS

Ekman (1932) suggested that increasing temperature might produce a positive thermotaxis and negative phototaxis to lead the eel to the spawning area in the Atlantic ocean, but Lissmann (1954) has made the following analysis:

> Many attempts have been made to deduce from the hydrographical conditions which exist along the routes of migration any gradient of stimulation which may provide the road signs for the fish on their journey. For instance, it is known that not only the European and North American eels, but also species from Australia, New Zealand and Japan breed in warm water of relatively high salinity. From the breeding ground a warm current of water sweeps towards the continents inhabited by the eels. However, when we try to apply to all available data our knowledge of the sensory physiology of fish we come up against some major difficulties. If we accept that the eel may respond to temperature changes of 0.03°C. we do not know accurately how sudden such changes would have to be appreciated by the fish. Assuming that for every 100 metres an eel swims it can perceive this temperature difference of 0.03°C., then starting from a temperature of 10°C. it would find itself after 100 kilometers in water of 40°C.—in which it could not live. Even if we grant that eels may be ten times as sensitive as the most sensitive fish we know, most of them would still not get half-way to the breeding ground. Similar calculations can be made for salinity. Moreover, if both temperature and salinity are considered guiding factors, all the eels in the Mediterranean would remain permanently trapped. This argument also applies for the gradient of hydrostatic pressure.

While not denying that currents might be perceived, I can visualize a situation where they would be useful in orientation, one in which two water masses were adjacent to each other and where the fish could follow along the edges by moving ahead, or the reverse, in which they may perceive the differences in sheer on their right flank or their left flank. I must confess that I am skeptical of this ability for fishes of the width of salmon and eels. The convection cells at the interface of two ocean water masses would create a most confusing pattern.

If the fish were swimming within a water mass it could have no sense of being displaced unless there were a fixed visual or tactile feature in the environment (compare the experiences of balloonists in a cloud). On the other hand, the place of contact of two water masses might have differences in salinity, dissolved gases, and odor (Hasler, 1954), all of which could be perceived. Unpublished data from our laboratory satisfy us that the minnow can smell the difference between water from the Georges Bank and samples from the Sargasso Sea. Nevertheless the line of contact between water masses might act like the *sheer effect* in directing the fish along the edge of a water mass, and might stimulate it to enter, or to stay in the water mass it had been swimming in.

The sensing of salinity, gases, or odors at any one place at sea appear to me to be signals which would be more meaningful as appropriate cues for informing the fish that it is, for example, in a place to spawn, but not in giving it cues for directional orientation. To help in reaching a distant goal, the edge (sheer) effect presumes that the fish might follow the broader of two water masses, but it leaves unexplained what might direct it straight ahead or the reverse. One might assume that a response could exist for the fish to swim straight ahead by maintaining its position so that the stimuli of one water mass would continue to stimulate the sensory structures on the right flank while a different set of stimuli operated on the left flank. A reversal of the response at sexual maturity would make the fish reverse its course so as to keep these stimuli on the left.

To pursue this apparently far-fetched notion further:

If an eel were following the Gulf Stream to the Sargasso Sea such an explanation might apply. It might be conceivably stimulated by differences in sheer between the Gulf Stream and the water masses on each side. But more likely some chemical difference might also serve as signal, in which case by swimming straight ahead, with the odor of the Gulf Stream on the left, it could arrive in the vicinity of the spawning grounds of the Sargasso Sea.

The downstream migration of salmon is generally explained by displacement by the current, yet the details of the descent bring out the importance of

orientation to a variety of stimuli depending upon the stage of development of the young fish. Hoar (1954) has shown, for example, how young sockeye salmon maintain their position in the stream by day and by night at an early age, but subsequently no longer react to the stimuli which make it possible for them to retain their position in the stream, and are therefore displaced.

How do young sockeye salmon find the outlet of a lake in a river system they have lived in when they reach the age for seaward migration?

Much more knowledge is needed about the downstream migration of salmon in order to furnish us the information needed to direct young salmon around dams. Upon the development of such devices hangs the success of salvaging the runs of salmon now threatened with extinction. The mortalities of young salmon from going over the dams or through the turbines is very great but is still unexplained (Andrew, Kersey, and Johnson, 1955).

LIST OF LITERATURE

Andrew, F. J., L. R. Kersey, and P. C. Johnson. 1955. An investigation of the problem of guiding downstream-migrant salmon at dams. *Bull. Int. Pacif. Salm. Fish. Comm.*, 8: 1–65.

Andriashev, A. P. 1944. Contribution to the biology and feeding of some predatory fishes of the Black Sea. *C. R. (Doklady) Acad. Sci. U.R.S.S.*, N. S. 44(7): 292–294.

Anonymous. 1955. Salmon and steelhead trout are found along the northern fringe of the "Japanese current." A Fish and Wildlife Service assignment under the Int. N. Pacific Fish. Commission through chartered vessels Mitkof and Paragon Aug.–Sept. 1955. *Comm. Fish. Rev.*, 17(11): 35.

—— 1956. Steelhead trout captured 1300 miles from shore. A study under supervision of C. E. Atkinson, U. S. Fish and Wildlife Service, Seattle, Washington. *Sport Fish. Inst. Bull.*, 50: 67.

Aronson, L. R. 1951. Orientation and jumping behavior in the gobiid fish *Bathygobius soporator*. *Amer. Mus. Novit.*, 1486: 1–22.

Clarke, G. L. 1936. On the depth at which fish can see. *Ecology*, 17: 452–456.

Collins, G. B. 1952. Factors influencing the orientation of migrating anadromous fishes. *Fish. Bull. U. S.*, 52: 375–396. (Fish. Bull. No. 73).

Cooper, G. P. 1953. Population estimates of fish in Sugarloaf Lake, Washtenaw County, Michigan, and their exploitation by anglers. *Mich. Acad. Sci. Bull.*, 38: 163–186.

Deelder, C. L. 1952. On the migration of the elver (*Anguilla vulgaris* Turt.) at sea. *J. Cons. int. Explor. Mer*, 18: 187–218.

Diesselhorst, G. 1938. Hörversuche an Fischen ohne Weberschen Apparat. *Z. vergl. Physiol.*, 25: 748–783.

Ekman, S. 1932. Prinzipielles über die Wanderungen und die tiergeographische Stellung des europäischen Aales, *Anguilla anguilla* L. *Zoogeografica*, 1: 85–106.

Fontaine, M. and R. 1952. Migration fluviale anadrome du Saumon (*Salmo salar* L.) et gradient de salinité. *Ann. Sta. Cent. Hydrobiol. appl.*, 4: 339–346.

Frisch, K. von 1951. Orientierungsvermögen und Sprache der Bienen. *Naturwissenschaften*, 5: 105–112.

——, and M. Lindauer. 1954. Himmel und Erde in Konkurrenz bei der Orientierung der Bienen. *Naturwissenschaften*, 41: 245–253.

Goldsmith, Marie. 1914. Les reactions physiologiques et psychiques des poissons. *Bull. Inst. gén. psychol.*, 14: 97–228.

Grassi, B., and Calandruccio. 1897. Riproduzione e metamorforsi delle Anguille. *G. ital. Pesca aguicolt.*, No. 7–8. [From Scheuring, 1930].

Grundfest, H. 1932. The sensibility of the sun-fish, *Lepomis*, to monochromatic radiation of low intensities. *J. gen. Physiol.*, 15: 307–328.

Hasler, A. D. 1954. Odour perception and orientation in fishes. *J. Fish Res. Bd Can.*, 11: 107–129.

——. 1956. Influence of environmental reference points on learned orientation in fish (*Phoxinus*). *Z. vergl. Physiol.*, (in press).

——, and W. J. Wisby. 1951. Discrimination of stream odors by fishes and its relation to parent stream behavior. *Amer. Nat.*, 85: 223–238.

——, and J. R. Villemonte. 1953. Observations on the daily movements of fishes. *Science*, 118: 321–322.

Hayes, H. R. 1953. Artificial freshets and other factors controlling ascent and population of Atlantic salmon. *Bull. Fish. Res. Bd Can.*, 99: 1–40.

Hecht, S., S. Shlaer, and M. H. Pirenne. 1942. Energy, quanta and vision. *J. gen. Physiol.*, 25: 819–840.

Hoar, W. S. 1954. The behaviour of juvenile Pacific salmon, with particular reference to the sockeye (*Oncorhyncus nerka*). *J. Fish. Res. Bd Can.*, 11: 69–97.

Huntsman, A. G. 1939. Salmon for angling in the Margaree River. *Bull. Fish. Res. Bd Can.*, 57: 1–75.

John, K. R. 1956. Observations on the avoidance of obstacles by blind fishes. (Unpub. ms., Amer. Mus. nat. Hist.).

Kleerekoper, H., and E. C. Chagnon. 1954. Hearing in fish with special reference to *Semotilus atro-*

maculatus atromaculatus (Mitchill). *J. Fish. Res. Bd. Can.*, 11: 130–152.

KRAMER, G. 1952. Experiments on bird orientation. *Ibis*, 94: 265–285.

——. 1955. Ein weiterer Versuch, die Orientierung von Brieftauben durch jahreszeitliche Änderung der Sonnenhöhe zu beeinflussen. Gleichzeitig eine Kritik der Theorie des Versuchs. *J. Ornithol.*, 96: 173–185.

LARIMORE, R. W. 1952. Home pools and homing behavior of smallmouth black bass in Jordan Creek, Illinois. *Ill. nat. Hist. Surv. Biol., Note*, 28: 1–12.

LEIBOWITZ, H. W., NANCY A. MEYERS, and D. A. GRANT. 1955. Radial localization of single stimulus as a function of luminance and duration of exposure. *J. opt. Soc. Amer.*, 46: 76–78.

LISSMANN, H. W. 1954. Direction finding in fish. *Advanc. Sci., Lond.*, 11: 69–71.

LOWE, R. H. 1952. The influence of light and other factors on the seaward migration of the silver eel (*Anguilla anguilla* L.). *J. Anim. Ecol.*, 21: 275–309.

MÄÄR, A. 1947. Über die Aalwanderung im Baltischen Meer auf Grund der Wanderaalmarkierungsversuche im Finnischen und Livischen Meerbusen i.d.J. 1937–1939. *Medd. Undersökn Anst. Sötvattensfisk. Drottningholm*, 27: 1–56.

MATTHEWS, G. V. T. 1955. Animal migration (Abstract of a symposium on migration, Sec. D. (Zoology) Brit. Assoc.). *Nature, Lond.*, 176: 772–773.

NÜMANN, W. 1955. Vorläufige Ergebnisse der Markierungsexperimente an Pelamiden (*Sarda sarda*) in Türkischen Gewässern. *Publ. Istanbul Univ. Hidrobiol. Ser. B*, 2: 157–166.

POWERS, E. B., and R. T. CLARK. 1943. Further evidence on chemical factors affecting the migratory movements of fishes, especially the salmon. *Ecology*, 24: 109–113.

SCHÄFFER, E. 1919. Der Aal auf dem Lande. *Schweiz. Fisch. Zg.*, 27: 79–80. [From *Kosmos* Nr. 3/4, Stuttgart, 1919].

SCHEER, B. T. 1939. Homing instinct in salmon. *Quart. Rev. Biol.*, 14: 408–430.

SCHEURING, L. 1929. Die Wanderungen der Fische. I. *Ergebn. Biol.*, 5: 405–691.

——. 1930. Die Wanderungen der Fische. II. *Ergebn. Biol.*, 6: 4–304.

SCHMIDT, J. 1906. Contributions to the life-history of the eel. *Rapp. Cons. int. Explor. Mer*, 5: 137–264; 267–273.

SHAPOVALOV, L. 1941. The homing instinct in trout and salmon. *Proc. 6 Pacif. Sci. Congr.*, 3: 317–322.

——, and A. C. TAFT. 1954. The life histories of the steelhead rainbow trout (*Salmo gairdneri gairdneri*) and silver salmon (*Oncorhyncus kisutch*). *Fish. Bull., Sacramento*, 98: 1–375.

SHOEMAKER, H. H. 1952. Fish home areas of Lake Myosotis, New York. *Copeia*, 1952: 83–87.

TALBOT, G. B. 1954. Factors associated with fluctuations in abundance of Hudson River shad. *Fish. Bull. U. S.*, 56: 373–413.

UZUKA, K. 1934. Some notes on the behaviour of the catfish *Parasilurus asotus*, as seen through the responses to weak electric currents. *Sci. Rep. Tôhoku Univ.*, Biol. Ser. 4, 8: 369–381.

VERWEY, J. 1949. Migration in birds and fishes. *Bijdr. Dierk.*, 28: 477–508.

WALLS, C. L. 1941. *The Vertebrate Eye.* 785 pp., Cranbrook Inst. of Science, Cranbrook Hills, Mich.

WESTENBERG, J. 1953. Acoustical aspects of some Indonesian fisheries. *J. Cons. int. Explor. Mer*, 18: 321–325.

WHITNEY, L. V. 1941. The angular distribution of characteristic diffuse light in natural waters. *J. Mar. Res.*, 4: 122–131.

WISBY, W. J., and A. D. HASLER. 1954. Effect of olfactory occlusion on migrating silver salmon (*O. kisutch*). *J. Fish. Res. Bd Can.*, 11: 472–478.

NEW BIOLOGICAL BOOKS

The aim of this department is to give the reader brief indications of the character, the content, and the value of new books in the various fields of Biology. In addition there will occasionally appear one longer critical review of a book of special significance. Authors and publishers of biological books should bear in mind that THE QUARTERLY REVIEW OF BIOLOGY *can notice in this department only such books as come to the office of the editor. The absence of a book, therefore, from the following and subsequent lists only means that we have not received it. All material for notice in this department should be addressed to H. B. Glass, Associate Editor of* THE QUARTERLY REVIEW OF BIOLOGY, *Department of Biology, The Johns Hopkins University, Baltimore 18, Maryland, U. S. A.*

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GENERAL BIOLOGY: PHILOSOPHY AND EDUCATION

INTERNATIONAL ENCYCLOPEDIA OF UNIFIED SCIENCE. *Volume I, Part 1, Nos. 1–5; Part 2, Nos. 6–10. Edited by Otto Neurath, Rudolf Carnap, and Charles Morris. The University of Chicago Press, Chicago.* Part I: $6.00; Part 2, $6.00; the set, $11.00. (1) x + 340 pp.; (2) vi + pp. 341–760 pp.; ill. 1955.

The work now published in collected form appeared years ago in a well-known series of paper-bound monographs, the first ten of which are collected in the above two volumes. The original monographs were uneven in quality and level of analysis, and they still are. The late editor makes the alarming statement that the encyclopedia is to be constructed like an onion, of which the first twenty pamphlets will constitute the heart. On the whole, it strikes the reviewer that the average reader will gain more from certain individual essays in these volumes than from any struggle to grasp the notion of Unified Science. These essays, their authors, and individual lengths are: Vol. 1, Part 1: Unified Science as Encyclopedic Integration, Otto Neurath, 27 pp.; Analysis and Synthesis in Science, Niels Bohr, 1 p.; Unity of Science as a Social Problem, John Dewey, 10 pp.; On the Importance of Logical Form, Bertrand Russell, 3 pp.; Logical Foundations of the Unity of Science, Rudolf Carnap, 122 pp.; Scientific Empiricism, Charles W. Morris, 13 pp.; Foundations of the Theory of Signs, Charles W. Morris, 60 pp.; Foundations of Logic and Mathematics, Rudolf Carnap, 72 pp.; Linguistic Aspects of Science, Leonard Bloomfield, 65 pp.; Procedures of Empirical Science, Victor F. Lenzen, 59 pp. Vol. 1, Part 2: Principles of the Theory of Probability, Ernest Nagel, 80 pp.; Foundations of Physics, Philipp Frank, 81 pp.; Cosmology, E. Finley-Freundlich, 60 pp.; Foundations of Biology, Felix Mainx, 97 pp.; The Conceptual Framework of Psychology, Egan Brusnwik, 105 pp. I am personally undoubtedly prejudiced by my tendency to regard articles which may be perfectly good sociology or philosophy merely as bad history. Still, a fundamental necessity for thinking about science on a broad scale is a firm understanding of the science itself and a solid knowledge of the history of its concepts. Speculatory unification always runs the risk of learning nothing because it understands everything too soon. The editor's idea that an encyclopedia rather than a system avoids the blight of a "superscience" of unification is not entirely convincing, since the whole tenor of the project seems to be based on the hope that some essential compatibility between the most varied sciences will emerge in time. This essence is presumably the seed from which will grow the super-onion of Unified Science. It is perhaps unfair

to deal in this manner with a program that has produced so many interesting and valuable single studies. As the editor remarks, that is all he hoped for, and we are in his debt for provoking and assembling them.

PAUL CRANEFIELD

SCIENCE AND MODERN LIFE.

By E. John Russell. Philosophical Library, New York. $2.75. iv + 101 pp. 1955.

This rather small book represents an expansion of the Beckley Trust Lecture for 1955. The author's intent is to state the important problems arising from the impact of science on daily life. The contents may probably best be illustrated by listing, in order, the headings of the sections following the historical introduction. They are as follows: Overwhelming Speed of Scientific and Technological Advance. Stability of Craftsmanship. Increasing Demand for Products. The Increasing Rate of Consumption of Natural Resources. More Leisure: How Shall it be Used? The Extension of Ownership of the Machine. The Change in Age Structure of the Population. The Lengthening of Average Life: Our Ageing Population. Is Our Population Changing in Quality? The Growing World Population: How Can it be Fed? Science and Social Organization. Atoms and Electrons: Revolutionary Possibilities. Mass Psychology and Mind Control and Forecasts of the Future: Gloomy Pictures. Will there Come an End to Scientific Discovery? Lost in the Gloom of Uninspired Research. The Scientist's Dilemma: Should he Continue Making Discoveries in View of their Possible Misuse? The Archbishop of York: His View. The Changed Relations of Science and Religion. Inadequacy of Science as a Complete Guide. The Great Question.

The great question to one reader is whether so great a number of topics of such magnitude can be treated adequately in a hundred pages of small format.

JANE OPPENHEIMER

MODERN SCIENCE AND GOD.

By P. J. McLaughlin. Philosophical Library, New York. $2.75. 90 pp. 1954.

The Pontifical Academy of Science traces its origin to the Accademia dei Lincei founded in 1603. On the 22nd of November, 1951, to mark the commencement of the academic year, His Holiness Pope Pius XII delivered an address in Italian to the members of this academy. The English translation of that address, first published in 1952, was reprinted in 1954. This volume consists of a translation of the text of the address and a paragraph-by-paragraph analysis directed to the reader who does not wish for "elaborate philosophical or scientific treatment, but would welcome a little of either or of both." The address itself is concerned principally with inquiring whether scientific discoveries strengthen or weaken those traditional arguments for God's existence which have a physical basis, especially those arguments which are concerned with *change* and *direction of change* in Nature. The conclusion is that the idea of God is confirmed and enlarged by new discoveries, especially in the field of the physical sciences.

Readers who are interested in the address itself may be more than a little annoyed at the interpolated comments; however, the book is so arranged that such readers may skip the comments and peruse the address with some feeling of continuity. This book is particularly recommended for reading by those who still believe that the official attitude of the Church toward science is pre-Copernican.

V. G. DETHIER

GENERAL BIOLOGY.

By Gordon Alexander. Thomas Y. Crowell Company, New York. $6.75. xiv + 881 pp.; ill. 1956.

BIOLOGY.

By Relis B. Brown. D. C. Heath & Company, Boston. $6.50. viii + 658 pp.; ill. 1956.

GENERAL BIOLOGY.

By Willis H. Johnson, Richard A. Laubengayer, and Louis E. DeLanney. Henry Holt & Company, New York. $6.95. x + 618 pp.; ill. 1956.

GENERAL BIOLOGY.

By Harrington Wells and Patrick H. Wells. McGraw-Hill Book Company, New York, Toronto, and London. $6.50. x + 520 pp.; text ill. 1956.

The publication of four new general biology textbooks could mean one of two things: either that the authors are dissatisfied with existing texts, or that the field is sufficiently lucrative to attract those who have a reasonably well-developed faculty for exposition. It is difficult to believe that the former situation holds, there being a number of good up-to-date textbooks already available which differ but little from any of those listed above. Let me, however, cast no aspersions, even if the sole purpose of writing be monetary; it is an honorable art, and there are few teachers who have no use for the proceeds thereof. Furthermore, the four volumes represent substantial efforts, and each adequately surveys biology in all of its aspects. The volume by Wells and Wells rates a nod over the other three, however, if only because it begins with an excellent discussion of evolution and keeps this central idea before the student at all times. Brown makes use of an interesting arrangement of text and illustrations. Many of the latter are provided with an olive-tan background that is quite attractive, and the pages are so arranged that a very wide margin permits the addition of student notes to supplement the textual material. The remaining two

books, while the subject is competently handled, have no outstanding or distinguishing characteristics.

C. P. SWANSON

BIOLOGY: HISTORY AND BIOGRAPHY

POMP AND PESTILENCE. *Infectious Disease, Its Origins and Conquest.*

By Ronald Hare. The Philosophical Library, New York. $5.75. 224 pp. 1955.

This book is a historical survey of disease and public health in which many topics are touched upon in an urbane and informative fashion. It is a popular work, but one which may be read with interest by historians of medicine if only for its amusing asides. The author treats of paleopathology, endemic and epidemic disease, and the germ theory. In the chapter Miasmas or Microbes, he gives an account of Hippocratic theory which makes it clear that it was neither stupidity nor superstition which allowed its acceptance for so long. The chapter, The Reaction of the Community, is a rather enthusiastic survey of sewage disposal and public health measures, while The Reaction of the Individual takes a reserved view of the merits of personal hygiene (as a means to maintain health, at any rate). The author has provided a good bibliography of both compilations and source material in public health and the history of disease. The book is absurdly overpriced, and buyers may well watch for it as a remainder. The quality of production is that associated with a book designed to sell at 12s. 6d. in England and about $2.75 here.

PAUL CRANEFIELD

LEONARDO THE ANATOMIST. *Logan Clendening Lectures on the History and Philosophy of Medicine. Fourth Series.*

By Elmer Belt. University of Kansas Press, Lawrence. $2.00. vi + 76 pp.; ill. 1955.

FROM WITCHCRAFT TO ANTISEPSIS: A STUDY IN ANTITHESIS. *Logan Clendening Lectures on the History and Philosophy of Medicine. Fifth Series.*

By Douglas Guthrie. University of Kansas Press, Lawrence. $1.50. x + 53 pp.; ill. 1955.

The fourth and fifth series of the Logan Clendening Lectures continue to reflect the skill used in choosing the lecturers. The first three lectures in the series were given by John Fulton, Chauncey Leake, and George Sarton, and the new volumes are a pleasing continuation. Elmer Belt's first lecture is a survey of Leonardo da Vinci's general achievements as an anatomist, and his second lecture deals in more detail with Leonardo's studies of the genito-urinary system. Belt brings his knowledge as a specialist in urology to this problem. Both lectures are illustrated.

Douglas Guthrie has given two lectures, each very interesting in itself. While it is no doubt true that we may, as he says, learn from each one some lessons of value in modern medicine, it is unfortunate that he has not developed for us a more detailed comparison and contrast between the two subjects. As it is, the reader is left with the thought-provoking task of comparing for himself the lecture on Witches and Witch-Doctors with that on Lister and His Achievement.

PAUL CRANEFIELD

A CHECK LIST OF THE E. DEGOLYER COLLECTION IN THE HISTORY OF SCIENCE AND TECHNOLOGY AS OF AUGUST 1, 1954.

Compiled by Arthur McAnally and Duane H. D. Roller. University of Oklahoma Press, Norman. $3.00 (paper). vi + 128 pp. 1954.

The collection catalogued in this volume is at the University of Oklahoma. According to the Preface, "persons interested in the history of science and technology and related fields are cordially invited to make use of the De Golyer Collection." The collection has undoubtedly grown since the appearance of the catalogue, and various gaps in it are probably more the result of the unavailability of certain works than of any oversight in purchasing. The University of Oklahoma is to be congratulated on possessing a collection which shows signs of developing into a major and valuable research library, and the reviewer, at least, envies Mr. Roller and Mr. De Golyer the pleasure of assembling it. The collection includes some fine Galileo items and the 1791 and 1792 editions of Galvani.

PAUL CRANEFIELD

A CATALOGUE AND HISTORICAL ACCOUNT OF THE BANKS SHELL COLLECTION. *Bull. Brit. Mus. (nat. Hist.), hist. Ser., Vol. 1, No. 3.*

By Guy L. Wilkins. The British Museum (Natural History), London. £1 (paper). Pp. 69–119 + 6 pl. 1955.

This is a sequel to an earlier work by the same author, already reviewed in these columns (*Q.R.B.*, 30: 68. 1955), and dealing with the Sloane collection. The present work provides the more interesting reading, owing to the difference in approach of the two collectors.

Sir Hans Sloane's collection was largely the result of his own personal efforts. It contained little in common with older collections and still less that was destined to find its way into later ones. Sir Hans was one of the founders of the British Museum—indeed, it is not going too far to say that he was the founder of that Institu-

tion. He maintained his own collections chiefly as feeders for the Museum and as soon as they received the curatorial attention that they merited, he began to deposit them there. Except for some limited material which he acquired late in life, his collections have had but these two owners, the British Museum and Sir Hans himself.

The collection of Sir Joseph Banks developed along entirely different lines. Sir Joseph was primarily a botanist, and it was as such that he was appointed to accompany Captain James Cook on his voyage around the world on the "Endeavor" and Captain Constantine Phipps on his voyage to Labrador and Newfoundland. Because the facilities for scientific research on these voyages were financed almost entirely from his own pocket, he came to appreciate the importance of gathering every kind of natural history that came to hand, with the result that not only shells, but also corals, insects, birds, minerals, etc., all found their way into his omnivorous packing cases.

The curatorial oversight of so much material was well beyond the ability of one man, and Sir Joseph came to depend upon his assistant, Daniel Charles Solander, who had been a student under Linnaeus at Uppsala, and had taken his doctor's degree there. Everywhere Sir Joseph went, Solander was sure to go. The two were seen so often in each other's company that the author compares them to Boswell and Johnson.

Solander was also employed as part-time custodian of the collections of Margaret Cavendish, Duchess of Portland. This gave him the opportunity to make exchanges of duplicate material between the two, and thus to strengthen both collections. Although the editors of the *Encyclopedia Britannica* do not consider Margaret Cavendish worthy of mention in their pages, she was the most generous patron of the arts and sciences of her day. The principal item in her collections was the Barberini vase which she purchased from Sir William Hamilton, from whom Solander obtained material from the Mediterranean area. The vase had been discovered in the sarcophagus of Alexander Severus, although modern critics consider it to be several centuries older than that association would indicate.

Another collector with whom Solander negotiated exchanges was Dr. John Fothergill, the man with whom Benjamin Franklin played chess by correspondence. On one occasion Dr. Fothergill was called upon to adjudicate the ownership of the Parkinson collection. Sydney Parkinson, a brilliant young artist employed by Sir Joseph Banks, died at an early age from a tropical disease. His collection was claimed by his feeble-minded brother Stansfield Parkinson, who seems to have been his residuary legatee, but Sir Joseph also claimed it as the work of his employee. Dr. Fothergill resolved the controversy by purchasing the collection and incorporating it in his own. Thomas Martyn examined the collection and testified as to its value, but it was certainly not worth what Dr. Fothergill had to pay for it, as he paid both claimants their demands in full. The combined Fothergill and Parkinson collections were subsequently purchased by Dr. William Hunter for the Hunterian Museum, and upon the death of the famous surgeon they became the property of the University of Glasgow, which is as far as their history can be traced.

As one reads of the activities of Solander in building up the Banks collection, one is struck by the large number of men of letters who, in addition to their other and better known activities, also collected shells. Among these we meet Dr. Henry Smeathmann, who sought to colonize Sierra Leone with emancipated Negroes about half a century before the foundation of Liberia; Baron Mulgrave, who commanded the North Polar Expedition on which Admiral Nelson began his career as a midshipman; Commodore John Byron, grandfather of the poet, who searched vainly for the Northwest Passage and became governor of Newfoundland; and many others.

The Linnaean Society, which eventually became the proprietor of the Banks collection, was privately owned and operated and did not have the financial resources to give adequate supervision to the material entrusted to it. Eventually the Banks collection was offered to the British Museum, which failed to appreciate its value, and accepted only a single cabinet containing but seven drawers of specimens. The remainder of the collection was dispersed at a public auction and cannot be traced. Consequently the author of the present work obtained more data from the Solander manuscripts in the library of the British Museum than from the shells themselves.

None of these manuscripts have ever been published, but many of them were consulted by later writers who leaned heavily upon them without giving Solander credit for the material which they lifted in wholesale quantities from his writings. Among these writers were Martyn, Bruguière, Humphrey, Bolten, Röding, and Lamarck. In pleasing contrast to these stands Dillwyn, who acknowledged freely his great debt to Solander, and cited him as authority for all names taken from his manuscripts.

A few years ago, when Dr. William H. Dall attempted to identify Solander's American species, he worked entirely from Dillwyn's book and the anonymous *Portland Catalog*, both of which were compiled from the Solander manuscripts. Apparently Dall did not know that the manuscripts were still in existence, for he ignored them completely, although he knew that they had been available to other writers, and he accepted Humphrey as the compiler of the *Portland Catalog* on Dillwyn's statement. I would myself question the wisdom of attributing the nomenclatorial terms originating in this work to Humphrey, whose name does not appear in it, and whose connection with it was not suspected until Dillwyn identified the author in the following century.

It is unfortunate that a work into which so much scholarship and painstaking research has gone should be marred by those two defects that an author always risks when he submits a manuscript—too much editing and too little proof-reading. The evidence of over-editing appears in the inconsistencies in the systematic part of the work. The names of Linnaeus and Bruguière are sometimes given in full and sometimes abbreviated. Some of the names in Thomas Martyn's *Universal Conchologist* are rejected and others are accepted. The names *Erosaria* and *Palmadusta* are treated as subgenera of *Cypraea* on some pages and are given independent generic standing on others. The names *Pilar* and *Pilaria* are alternative forms of the same name; the former is a vernacular word in a native African dialect and the latter an attempt at Latinization. A case might be made out for the use of either one, but not for both. Yet the two forms are used indiscriminately. It is inconceivable to me (knowing the author personally) that the latter could have perpetrated such sloppy work. It seems more likely that the manuscript was consistent when submitted, but that it fell a victim to an editor who had that little learning which is considered a dangerous thing, and a desire to have a finger in the pie, and who took the liberty of making changes in the manuscript, but did not examine the manuscript carefully to ensure that the changes were made consistently in each instance.

The inadequacy of the proof-reading is evidenced by the misspellings of the generic names *Austropteria*, *Haminoea*, *Latirus*, *Lionconcha*, *Philine*, and *Pterorytis*, as well as the surnames of Helbling and the present reviewer. Had the writer read the proof these errors would surely have been avoided. There are a few other errors of a taxonomic and nomenclatorial nature, but not of vital importance. The work has a splendid bibliography of 91 items, but the lack of an index is truly unfortunate.

JOSHUA L. BAILY, JR.

EARLY AMERICAN SCIENCE NEEDS AND OPPORTUNITIES FOR STUDY.

By Whitfield J. Bell, Jr. Institute of Early American History and Culture, Williamsburg. $1.25. x + 85 pp. 1955.

The author has contributed a stimulating analysis of the reasons for the neglect of science by American historians and a challenging plea for more research in the history of early American science by them. His major thesis is that science forms an integral part of the cultural history of America, and his minor thesis, that prior to 1820 American science was so simple and easy to follow that historians need not be deterred from studying it even if they lack a profound knowledge of science. The conclusion drawn is that a valuable contribution to the history of the United States may be made by providing biographies of early American scientists and by studying their relationships with European scientists. The bibliography of fifty early American scientists which is provided will no doubt stimulate such studies.

The author points out that there is a hiatus in documentary material, caused by a tendency to save only documents related to political and military personages. This plea for the preservation of such material, and for the initiation of such studies is timely and welcome. On the other hand, the author seems to imply that no deep knowledge of science is necessary for the undertaking he proposes. In Butterfield's Preface the statement is made that the author "writes spiritedly even when listing works by and about a scientific author," as if nothing could be intrinsically more dispiriting. Bell himself says that the Index-Catalogue contains "much besides long lists of articles on carcinoma and the common cold."

It is not, in my own opinion, possible to write studies in the history of science in which every aspect of the scientist is studied save only the scientific content and scientific significance of his work. Even the contemporary reaction of other scientists cannot be evaluated or taken as a measure of the man's work unless the historian himself understands the science in question. The highest type of history of science, in which the scientist's work is related to all of the forces of his time, can be written only after the significance of his scientific work has been understood, and the specious similarity between such efforts and the cultural-history approach should not be allowed to obscure the difference between the two. In no way to deprecate the great value of the program Bell proposes, one yet feels compelled to emphasize that this aspect of cultural history is just that, and is not in fact the history of science. Hamlet is still a rather deeper play when the Prince of Denmark is in the cast: though admittedly a harder play to understand and expound. The author is clearly aware of this fact, and is chiefly concerned to let other historians know that certain aspects of the role of science in our cultural history are within their grasp. It is all the more unfortunate that such a statement as the one that "Science was not yet compartmentalized, each tight little box jealously guarded by guildsmen who talked to themselves and one another in a private jargon" is allowed to suggest a historian's resentment that science has become so hard to cope with. We must applaud the effort to bring historians into those areas of the history of science where they may operate with reasonable safety even if we secretly have a greater admiration for the catastrophic but at least heroic struggles of Henry Adams or the successful efforts of men trained both in history *and* in science.

PAUL CRANEFIELD

THE YOUNG NATURALIST

MODERN BIOLOGY.

By Truman J. Moon, Paul B. Mann, and James H. Otto. Henry Holt & Company, New York. $4.88. x + 757 pp. + 14 pl.; text ill. 1956.

BIOLOGY FOR YOU. *Third Edition.*

By B. B. Vance and D. F. Miller; in consultation with W. R. Teeters. J. B. Lippincott Company, Chicago, Philadelphia, and New York. $4.20. 652 pp.; ill. 1954.

Both of these textbooks do an excellent job of presenting biology in all of its modern aspects to high school students. There is no concession to the mediocre, both are readable and lively, the illustrations on the whole are clear and closely tied to the text, and summaries, questions, and problems point up the significance of each chapter. If the student can absorb the contents of either volume, he should have a good start and a firm foundation for collegiate studise in biology; and if these books represent a terminus in biological training, the student should be able to derive an understanding and appreciation of newer developments. The volumes differ from each other in their arrangement of the subject matter, but both are worthy of recommendation.

C. P. SWANSON

ECOLOGY AND NATURAL HISTORY

THE CHEMISTRY AND FERTILITY OF SEA WATERS.

By H. W. Harvey. Cambridge at the University Press, London; [*Cambridge University Press, New York.*] $5.50. viii + 224 pp.; ill. 1955.

This book forms a continuation of two earlier books by the same author, the first being *Biological Chemistry and Physics of Sea Water* (1928), and the second, *Recent Advances in the Chemistry and Biology of Sea Water* (1945). In the present volume the author has retained many of the features of the older works, especially the 1945 volume, yet has expanded, added, and modified in keeping with the results of research carried out during the past ten years.

The book is divided into two parts: Part I, The Environment of the Flora and Fauna, and Part II, The Chemistry of Sea Water. This division emphasizes the two broad fields of study indicated in the title. Part I deals primarily with the chemical, physical, and biological properties of the oceans that control and reflect the spatial and temporal changes in the fertility of the seas. The first chapter, on the Composition of Sea Water, is a very brief general statement (6½ pp.) concerning the chemical properties of ocean waters. This chapter, together with Part II of the book, provides an adequate description of the chemical features of the marine environment. Chapter II, Mixing and Lateral Transport, is a highly abbreviated account of some of the major circulation features in parts of the oceans. This chapter is the only dark spot in an otherwise bright picture. To be sure, a full discussion of oceanic circulation would require more space than the entire present volume and would be inappropriate in a work concerned primarily with the chemistry and fertility of the seas. Nevertheless, a simplified discussion of the circulation in only the Atlantic Ocean, the English Channel, and the Tees estuary does neglect important parts of the marine environment—parts that have unique circulation features important to the distribution of chemical properties and to the fertility of the regions.

Chapters III through VI, which complete Part I, develop very well the problems encountered in studying the fertility of the seas. Chapter III, Changes in Composition Due to Plants and Animals, summarizes the changes in chemical composition of the marine environment that occur during phytoplankton and zooplankton production. The results of measurements in the oceans as well as in vitro are brought together to illustrate the cycles of carbon, nitrogen, and phosphorus from the environment through the biota. The chapter on Changes in Composition Due to Bacteria summarizes the many functions of the bacteria. The last two chapters of Part I, on Factors Influencing the Growth of Plants, and Interrelations Between Plant Production and Animal Communities, when taken together, are essentially an outline of the basic information, taken from both field and laboratory studies, that forms the substance of marine ecology.

Part II, The Chemistry of Sea Water, is a somewhat expanded version of Chapters 2 through 6 of the author's 1945 book.

Throughout the present volume the author demonstrates his ability to convey ideas in a few words. The book, therefore, is brief. The author, admittedly, has made no attempt to assemble a complete bibliography on each subject. His references are "limited to the more recent papers dealing with the various subjects." The book will be useful as a source of concepts and ideas, but not as a bibliography to the literature of oceanic sciences.

DAYTON E. CARRITT

CLIMATES IN MINIATURE. *A Study of Micro-Climate and Environment.*

By T. Bedford Franklin. Philosophical Library, New York. $3.75. 137 pp. + 8 pl.; text ill. 1955.

Here is a delightful book. Since it is not intended as a technical treatise of micro-climatology, the professional scientist should not apply a technical yardstick in his judgment of it. Even though it is written primarily for the layman it is well worth the attention of the professional. The author has devoted a lifetime to his avoca-

tion of micro-climatology and gardening. To this pursuit he has brought enthusiasm, curiosity, and a full appreciation of scientific method and accomplishment. The chapter on the relations between soil and microclimate and their effects on cranberries in Wisconsin and Cape Cod is just one example of the manner in which the author utilizes his scientific knowledge in the telling of his story. Other chapters are concerned with anecdotes and the descriptions of field experiments relating to such diverse phenomena as temperature changes in the burrows of hibernating rabbits, the intelligent treatment of clay soils in gardening, the effect of walls on the survival and fruiting of plants in severe climates, the fate of rain once it hits the ground, the measurement of frost, the insulating effect of snow, and the heating of homes. The entire book is written in a warm, informal style which makes for pleasant informative reading.

V. G. DETHIER

THE BARREN GROUND CARIBOU OF KEEWATIN. *U. Kans. Mus. nat. Hist., misc. Publ. 6.*

By Francis Harper. University of Kansas, Lawrence; [Arctic Institute of North America, Washington]. $1.50 (paper). ii + 163 pp.; ill. 1955.

Francis Harper visited the Wind River area of Keewatin, Northwest Territory, in 1947 primarily to observe the barren ground caribou, *Rangifer arcticus arcticus*. This book is a well-organized report of his observations, which, with well-documented supporting data from other publications and observations of long-time residents of the region, is a monograph of the species as it exists today.

Harper describes the spring movement to the north and the return south in the fall, and a curious retrograde September migration, which can at present only be tentatively explained as the expression of an innate preference for the tundra when insects and other factors do not force the animals southward into the forests.

Most of the text is devoted to the ecology of the animals, both in their relations to man, and to the natural aspects of their environment. It is evident that Harper considers human exploitation as the most serious factor in affecting the present numbers of the animals, but the effects of all biological relationships are carefully covered, including those with free-living insects and ectoparasites as well as those with other vertebrates. The advisability as well as the practicability of introducing Asiatic Reindeer into the area is seriously questioned.

Students of the social behavior of mammals will enjoy the documentation of the way in which these animals live, their disposition, the social structure of the herds, their food preferences, and the activity of the rutting season. The latter begins in mid-October, and at that time the herds tend to be large. The sex ratio, 1:10 in these large herds, indicates polygamy. Fawning did not occur in the region studied, but fawns in August and September were observed with antlers 1–2 inches in length.

The closing section of the book deals with morphology and taxonomy. There is more of the former, covering pelage, molt, foot-glands, mastology, and geographical variation, but there is no synopsis of the species or subspecies in the conventional sense. Each section of the text is extensively indexed with references, and there is a long list of literature citations. Anyone interested in the biology of the Arctic will find this book essential reading.

BRYAN P. GLASS

AN AUSTRALIAN ANIMAL BOOK.

By Charles Barrett. Oxford University Press, Geoffrey Cumberlege, Melbourne, and Wellington; [Oxford University Press, New York.] $3.60. xii + 325 pp. + 65 pl. 1955.

This book is a most fascinating account of the vertebrate life of the Australian subcontinent. Here are the natural history notes of one who has spent a lifetime in their accumulation. The book is arranged systematically, beginning with the mammals, but the emphasis is on natural history and habits, not on systematics, and the language used is lay language.

The first third of the book is devoted to the mammals, and most of the rest to birds. Reptiles, amphibians, and fishes are covered only briefly. The author has quoted extensively from other books, and from his personal correspondence with the numerous Australian naturalists who have contributed to his knowledge of the Australian fauna. Six pages are devoted to cataloguing the folly of the acclimatizing experiments of the past century, and the effects of exotic introductions are noted throughout the book, together with the environmental modifications wrought by colonization and agriculture. "... Formerly common, but now rare except in restricted areas ..." seems to be the refrain of the book, and the author rightly expresses concern for the future of many of the species he describes.

Biologists may prickle a bit over the author's apparent preference for the "habit precedes structure" theory. However, this doctrine is not preached throughout, and the wealth of natural history information is too important for the book to warrant censure on this one point alone.

To Australians this book should be a handy guide to nature, and a stimulus to a greater pride in and concern for their unique natural history inheritance. To us who may never be privileged to view at firsthand the natural wonders described, the book is a treasure of information and illustration that will be useful both as

a technical reference and as a pleasurable experience in natural history reading.

BRYAN P. GLASS

EVOLUTION

THE PYRAMIDELLID MOLLUSKS OF THE PLIOCENE DEPOSITS OF NORTH ST. PETERSBURG, FLORIDA. *Smithson. misc. Coll., Vol. 125, No. 2. Pub. 4186.*

By Paul Bartsch. Smithsonian Institution, Washington. $1.40 (paper). iv + 102 pp. + 18 pl. 1955.

One of the most important recent changes in macrotaxonomy has been the transfer of the family Pyramidellidae from the Prosobranchiata to the Opisthobranchiata. In all probability the Opisthobranchiata, as formerly understood, was a polyphyletic group, and while one of its subgroups was undoubtedly derived from the Pyramidellidae, this is not necessarily true of the order as a whole. Certain primitive elements in the Prosobranchiata, the Opisthobranchiata, and the Pulmonata form a compact group which might appropriately be constituted a fourth order of rank comparable to the other three, and which should include the Pyramidellidae.

From these observations, the importance of the Pyramidellidae from the standpoint of evolution becomes clear. In number of species it is one of the largest molluscan families, yet in the classical monograph of the family published nearly half a century ago, in which the author of the work here under consideration participated, only four genera were recognized. The species are all very minute (although certain primitive fossil species are said to be quite sizable), and unless examined microscopically the tremendous variety of the forms represented is likely to pass unnoticed.

In the present work the division of these four genera into new genera more in keeping with modern ideas of taxonomy has been carried to the extreme. It seems that the elevation of so many small groups to independent specific rank has been overdone, yet it must be admitted that if the shells were larger this multiplication of genera would probably seem natural enough. In any case it must be remembered that the author of this work is a painstaking scholar who knows what he has seen, and we should be thankful for his having made such a meticulous examination of a family that has never received the attention that its position in theoretic biology merits.

From the nomenclatorial standpoint the paper leaves much to be desired. The author has fallen back upon classical mythology for many of the names which he has given to his new species. Now when a proper name is converted into an adjective for specific use, the rules of the International Commission on Zoological Nomenclature provide that this shall be done by affixing the genitive terminations of the first and second declensions, even when the proper names have a classical genitive form of their own. Yet we meet with *Venusae* when we expect *Veneris*, *apolloi* when we expect *apollinis*, etc. The effect, of course, is quite ridiculous; the author must have formulated these names with his tongue in his cheek, possibly in order to discredit the Commission. It is to be hoped that the new code, which is scheduled for publication in the near future, will rectify this senseless provision.

The correct name of the genus which the author calls *Iobaea* is of course *Iolina*; the earlier name is preoccupied, and the name *Turbinella* (p. 26) is of course a typographical error for *Turbonilla*. The illustrations of the new species are excellent.

JOSHUA L. BAILY, JR.

GENETICS AND CYTOLOGY

THEORETICAL GENETICS.

By Richard B. Goldschmidt. University of California Press, Berkeley and Los Angeles. $8.50. x + 563 pp.; ill. 1955.

In biology—Goldschmidt stresses at the beginning of this remarkable book—theorizing is limited; in fact, it is seldom practiced except in immediate relation with a particular piece of research. This book is an attempt to fill this gap as regards genetics. Welcome and most valuable as this effort is, let us hope that it will not encourage in genetics a phase like that through which physics went about 30 years ago. The theoretical physicist was then, for a short time, a sort of armchair wizard with a snob value well above that of the experimentalist. Nowadays the theoretical physicist is not obviously distinguishable in manners and prestige from any other specialized physicist. We do not want such a phase in genetics. There is a minor branch of theoretical genetics which has already placed itself on a pedestal: statistical genetics—incidentally ignored by this book. A good proportion of its lesser practitioners have already fallen for the attraction of mathematical exercise as a smoke-screen. The danger is not imaginary.

This book is a summary, and an up-to-date restatement of Goldschmidt's ideas expounded over a series of years. It is a landmark in the history of genetics likely to stand out long after Goldschmidt's ideas will have been partially accepted and partially discarded, just as *The Mechanism of Mendelian Heredity* still stands out in spite of the fact that we have gone beyond it.

The outstanding value of the substance of the book will make readers pardon its shortcomings in form. It is prolix and imprecise in language and it has not been edited carefully, perhaps due to the trying circumstances under which it was written and the enormous amount of information which it marshals.

Finally, its "I told you so" attitude, explicit or implicit throughout and mildly irritating even to those who agree with most of Goldschmidt's ideas, will not help to convince the others. Perhaps the author did not care to do so: the value of the book to genetics as a whole would have been greater if he had forgone this extra pleasure. This does not mean that Goldschmidt was not entitled to hit back, as he does repeatedly with his usual wit and vigor, where he had been misinterpreted.

The main idea of Goldschmidt is that the "genetic material" is organized in a series of hierarchical fields up to and including the whole chromosome. The spatial and structural relations of the parts of the chromosome determine the series of fields of activity, but one element can be part of more than one field. Mutation consists of a repatterning, by loss or rearrangement, submicroscopic or microscopic, of the chromosome structure.

This view gives a better interpretation than the classical theory of the corpuscular gene for the facts which have emerged in recent years especially from the analysis of minute regions of the chromosomes in *Drosophila*, *Aspergillus*, maize, bacteriophage, etc. The difficulties with the classical theory are mainly due to inconsistency when we try to identify a gene simultaneously as a unit of function, of crossing over, and of mutation. This identification is good enough at the crude levels of analysis, at which most of everyday normal genetics and all of applied genetics works. It is not good enough as soon as one inquires into the structure and function, i.e., the nature, of the genetic material. The inconsistency disappears to a large extent with Goldschmidt's approach.

While many of those who have recently inquired into the nature of the genetic material now broadly agree with Goldschmidt, there are certain details which are not wholly convincing. For instance, granted that a mutation is a change of "order or pattern on a supramolecular level within a section of chromosome . . . of not strictly delimited size" (p. 179), why should changes at the molecular level, be they of structure or of constitution, not also be included? It seems that a stress on pattern as the significant element should not lead one to ignore that a pattern arises from simpler ultimate elements, be they nucleotides, amino acids, or anything else. The pattern can therefore be changed also by changes in these ultimate elements, though for probability considerations this will admittedly be the exception rather than the rule.

It would be impossible to go into details about the book. Besides being very stimulating throughout, it contains an enormous mass of information, and perhaps some misinformation, and the significant relationships are brought out clearly. The two chapters on The Action of the Genetic Material and the Genetics of Sex Determination are enough by themselves for a new book on physiological genetics.

In conclusion, this book is a milestone in genetics. It cannot fail to provoke pleasure, irritation and a stiffening of outlook, or progressive thinking according to the views of different readers. One thing it cannot possibly do: leave the reader indifferent.

G. PONTECORVO

LETALFAKTOREN, *in Ihrer Bedeutung für Erbpathologie und Genphysiologie der Entwicklung.*

By Ernst Hadorn. Georg Thieme Verlag, Stuttgart; [Intercontinental Medical Book Corporation, New York]. DM 39.—; ($9.30). 338 pp.; ill. 1955.

Since the demise of the *Handbuch der Vererbungswissenschaft* there has been a paucity of new monographic surveys of particular areas of genetics. Most of the reviews in *Advances in Genetics* are too limited by requirements of space and are too strongly focused on recent developments to provide the type of comprehensive consideration of a subject we found in such monographs as that of Curt Stern on Crossing Over. The new book by Ernst Hadorn is cast in the mold of that great tradition of a thorough and comprehensive treatment of its topic. It is trebly welcome, first for that, second because of its stimulating quality in suggesting fresh experimental attacks on open problems, and third because this particular phase of genetics, the significance of the lethal mutant, has not been so treated previously.

Lethal factors are not essentially different in nature from non-lethal mutants. Most detectable mutants produce a damaging effect, and the lethal is simply more extreme. Consequently, a survey of lethal factors becomes a coverage of all genetical principles as exemplified in mutants of extreme effect. This is quite evident from a glance at the chapter headings, which deal with genetical methods of studying and maintaining lethals; the origin of lethals by mutation; the chromosomal basis of lethal mutants, especially deficiencies; dominant lethals; polygenic lethals; maternal predetermination and cytoplasmic inheritance; penetrance and expressivity; dominance and recessiveness; specificity as to developmental phase; cell and organ specificity; pleiotropic action; cell autonomy; phenocopy experiments; biochemical and physiological analyses of lethal action; therapy of lethal effects; practical effects in animal breeding; etc.

Hadorn is to be particularly congratulated on the care which he has taken to clarify and define the terminology of lethal, semilethal, subvital, and supervital mutants in terms of penetrance, as well as the perspicacity with which he has dealt with the possible interactions of genes and genetic systems in considering degree of expression, pleiotropy, phenocopy production, and differentiation. He has an open mind as to whether there is a corpuscular gene or whether, as Goldschmidt has been foremost in advocating, the entire chromosome

is the functional unit and the gene but an unnecessary abstraction; yet the discussion is couched in conventional terms of the gene, and Hadorn does not appear to believe that all mutations are position effects. Hadorn does not fall into the trap of identifying the "phenocritical" period during development when a particular external agent can produce a phenocopy with the time of action of the gene in question, and this is most heartening considering the amount of work done to produce and study phenocopies in Hadorn's own laboratory.

The book is filled with well-chosen examples, especially from *Drosophila*, mouse, and chicken, to illustrate each principle. The work of Hadorn and his students supplies some of the best of these, such as the *Drosophila* lethals *translucida*, *cryptocephala*, and *lethal-meander*; but it is characteristic of the book that while full use is made of the material with which the author has a first-hand acquaintance, he draws just as extensively on an exceedingly wide knowledge of the genetic literature. That, together with clarity, insight, and well-balanced judgment, are the prime characteristics of this book.

In advanced courses in genetics this book may very well be used together with *Genetics and Metabolism*, by R. R. Wagner and H. K. Mitchell, to provide a sufficiently comprehensive treatment of the field as a whole. The use of the German text will also help to prepare graduate students for their language examination—an extra bonus.

BENTLEY GLASS

ADVANCES IN GENETICS. *Volume VII.* *Edited by M. Demerec. Academic Press, New York.* $8.00. x + 309 pp.; ill. 1955.

The contents of *Advances in Genetics, Volume VII*, illustrate the diversity of present genetic investigations and their interrelationships with other fields of science. The volume begins with the problem of microbial drug resistance, discussed by Vernon Bryson and Waclaw Szybalski. The authors outline the possible origins of resistant bacterial cells owing to (1) spontaneous gene mutation occurring before the addition of the toxic agent, and with or without the phenomenon of phenomic lag; (2) mutation induced by the presence of the toxic drug itself or indirectly through the action of an environmental agent; or (3) a combination of these causes. In this work one realizes the extreme importance of new techniques, such as the Lederbergs' method of replica plating with velveteen. Loss or resistance occurs through reverse mutation or simply by removal of the drug or dilution, for often the drug-resistant cells are at a selective disadvantage. The authors describe briefly methods, used in multiple chemotherapy, which are of great value to the clinician.

The next two papers are of especial interest to students of speciation and evolution: The "Obscura Group" of the Genus *Drosophila*, by Adriano A. Buzzati-Traverso; and Chromosomal Polymorphism in the Diptera, by A. Brito da Cunha. The treatment of the "Obscura Group" is reminiscent of the thorough analysis given for other groups by Patterson and Stone. Especial attention is given to the Palaearctic members of this group, since previous authors have discussed the Nearctic members at some length. An interesting feature is the far greater number of chromosomal rearrangements in element "C" compared with the other chromosomes found in all the members of the group. In the second *Drosophila* paper, da Cunha reviews briefly the few cases of phenotypic polymorphism in *Drosophila* and devotes the bulk of his space to a consideration of chromosomal polymorphism chiefly in the form of paracentric inversion. Since only non-crossovers are recovered from paracentric inversion heterozygotes, this type of chromosomal rearrangement has a selective value and is retained in the wild population. The extensive studies of Dobzhansky and his colleagues on seasonal changes in inversion frequencies led to their experiments with population cages, in order to determine the adaptive values of the various gene sequences of different geographical (or altitudinal) regions at specific temperatures. There are a number of components, to some degree independent, of the adaptive value of a gene sequence: larval competition, longevity, fecundity, sexual activity, egg hatchability and differences in nutritional requirements. Work of this kind, I feel, contributes greatly to our understanding of the bases of natural selection. It might be suggested that relative size of population may be an important factor in determining the seasonal variation in the percentage of inversions found in Moscow populations of *D. funebris* when compared with a lack of seasonal change in percentage of inversions found in rural populations.

John A. Moore's article on Abnormal Combinations of Nuclear and Cytoplasmic Systems in Frogs and Toads deals with experimental embryology in species hybrids from the genetic point of view. Techniques permit obtaining gynogenetic haploids, diploids, and polyploids; gynogenetic hybrids; and androgenetic haploids and hybrids, as well as achromatic embryos. The observations based on these methods support the older views that the maternal genes acting during oogenesis are responsible for the course of development up to or near the beginning of gastrulation. There appears to be no irreversible limitation of genetic ability as far as late blastula nuclei.

The last two papers are concerned with organisms of economic importance: the domestic rabbit and barley. In Recent Genetics of the Domestic Rabbit, surveyed by Paul B. Sawin, one is impressed with the opportunities for studies of the genetic background of certain human pathological conditions afforded by a study of similar conditions in the rabbit. Recent work

on internal characters in the rabbit shows that many blood vessel anomalies as well as skeletal patterns depend upon a combination of a number of genes. Serological studies are not only of importance to medicine but give an opportunity to study fundamental gene activities. The Origin and Evolution of Cultivated Barley, by Ryuhei Takahasi, traces the phylogeny of barley from two wild forms, *Hordeum spontaneum*, found in Western Asia, and *Hordeum agriocrithon* in Tibet. The author uses historical evidence, comparative morphological studies, and a modification of Vavilov's Gene Center Theory. Takahasi thinks it probable that cultivated tough-rachis forms arose by mutation from both wild species of barley. Through hybridization of these tough-rachis forms, various 6-row and 2-row types have arisen, all with the tough rachis essential to the farmer. The ancestral home of barley is in great dispute among various authors. Takahasi favors central Asia.

Each paper in this volume possesses an extensive bibliography. A subject and author index for Volume VII as well as a cumulative subject index for Volumes I–VI are provided. This book is essential reading for any genetics research worker or teacher who wishes to keep informed about the progress in his field.

SARAH B. PIPKIN

THE CYTOLOGY AND LIFE-HISTORY OF BACTERIA. *Second Edition.*

By K. A. Bisset. The Williams & Wilkins Company, Baltimore. $6.00. xii + 164 pp.; ill. 1955.

This work is a reissue with occasional revisions of the first edition (*Q.R.B.*, 26: 290. 1951) which appeared in 1950. It remains a personalized account of the author's outlook on the structure and evolution of bacterial cells. His most generally credited contribution is the insistence (with Robinow and others) on the multicellularity of many apparently simple bacteria, and how this may confound cytological interpretation. His accounts of nuclear organization and fission and of diverse life cycles are more notoriously controversial. Particularly exceptionable is the implication that the generality of these accounts now finds genetic support, e.g., from the claims of trinucleate cells and regular autogamous fusion in *Escherichia coli*, or from the forms of sexuality in other species. All students are now agreed that bacteria are cellular and have nuclear structures, though they are divided on the existence of a typical mitotic apparatus and on the details of chromosomal organization. Unhappily, genetic studies have not been able to shed critical light on these questions; indeed, there is still lacking a *rigorous* demonstration (parallel to that for higher forms) of the genetic functions of the nuclear bodies. Until the details of mitosis and, hopefully, meiosis or their equivalents have been worked out for bacteria, with correlated genetic and cytological analysis, we shall have to continue to rely on plausibility more than rigor.

Fantastic beliefs in "branched chromosomes" would be rightly liable to criticism if anyone entertained them. Their repeated attribution in this work is probably based on a misconstrual of speculative proposals of branched linkage groups such as are the well-known consequences of chromosome-structural heterozygosis in *Drosophila* and maize.

The book cannot be accepted as a balanced prospect of the field of bacterial cytology, which quite likely is not amenable to such a treatment at this stage of its development. The work is a curious mixture of impressive fact and simple fancy, of beautiful photomicrographs and crude sketches, of reasoned criticism and flat dogma. Specialists in microbial cytology will find it a convenient résumé from one of its notable figures.

J. LEDERBERG

GENERAL AND SYSTEMATIC BOTANY

FERNS OF TENNESSEE, *with the Fern Allies Excluded.*

By Jesse M. Shaver. Bureau of Publications, George Peabody College for Teachers, Nashville. $6.00. xvi + 502 pp.; ill. 1954.

Among state fern floras, no other has such adequate illustrations or such full descriptions. Of 248 illustrations, 81 are half-tones and 54 are distribution maps. The remainder are detailed line drawings not only of the common types of ferns but often of unusual varieties or aberrant forms. The descriptions are complete, frequently including detailed discussions of the variations to be found in the taxa.

Although the list of ferns in Tennessee does not exceed 57 species and a few varieties and forms, it does include such diverse geographical elements as two filmy-ferns (*Trichomanes petersii* and *T. boschianum*) with tropical affinities, and the narrow beech fern (*Phegopteris connectilis*) which is most widely distributed to the north. Not only are the county ranges in Tennessee discussed but general distribution data, as given by Braun, are included.

The initial chapter, Some General Notes on Ferns, includes such diverse topics about ferns as folklore, nomenclature, the life cycle, gardening, making a herbarium, and growing ferns from spores, and will be of interest to the beginner, amateur, and professional alike. The book ends with a detailed list of exsiccatae studied, an adequate glossary, and indices to both Latin and common names of the Tennessee ferns.

The Preface includes corrections for most of the rather minor errors. It is surprising that there are so few mistakes when one considers that the book was produced by collecting and repaginating a series of articles in *The Journal of the Tennessee Academy of*

Science. The initial chapter gives data on the American Fern Society for 1942. Its annual dues are now $2.00 and the treasurer is Dr. Ronald L. McGregor, University of Kansas.

Keys to genera and species (prepared for only a few genera, e.g., *Cystopteris*) would have been desirable, but the illustrations and descriptions are such that no one will have difficulty in identifying Tennessee ferns.

AARON J. SHARP

BOTANY. *Third Edition.*

By Paul Weatherwax. W. B. Saunders Company, Philadelphia and London. $5.75. x + 509 pp.; ill. 1956.

GENERAL BOTANY.

By William T. Taylor and Richard J. Weber; illustrated by Wilma Riley. D. Van Nostrand Company, Princeton, Toronto, London, and New York. $5.75. viii + 376 pp.; ill. 1956.

Both of these texts follow a conventional pattern established long ago for one-semester botany courses. If there have been any innovations in illustration, approach, or emphasis, they must be subtle indeed, for they are not strikingly evident to the reader. Both treatments of the subject, however, are competent enough, the Weatherwax textbook being the more comprehensive, better planned, and more readable of the two. Perhaps this is due to the fact that it is in its third edition, and has had the advantage of time and several revisions. On the other hand, it does take one great step forward by introducing the student to evolution as a central, unifying concept early in the text rather than attaching it in the form of a last chapter, as in the text by Taylor and Weber. In such a position evolution is a dangling, unrelated, and unillustrated afterthought instead of being the warp that holds together, and makes meaningful, all the diversity that exists in the plant kingdom. One has the feeling that Taylor and Weber knew that evolution had to be mentioned sooner or later, but being uncertain of a proper time and place they postponed it to the last. Any student, whether he realizes it or not, has been intellectually deprived if exposed to a consideration of evolution in this manner.

C. P. SWANSON

ECONOMIC BOTANY

FRUITS OF HAWAII. *Description, Nutritive Value, and Use.*

By Carey D. Miller, Katherine Bazore, and Mary Bartow. University of Hawaii Press, Honolulu. $2.75. x + 196 pp.; ill. 1955.

The title of this book is somewhat misleading. It is true that the edible fruits of Hawaii form the principal subject matter, but the emphasis is strictly culinary rather than botanical, and the authors are home economists rather than economic botanists. This is not intended, however, as a deprecatory statement, for the book is a compendium of a great many enticing recipes in which these fruits form the principal ingredients. Among a host of less familiar species, the following fruits are mentioned: avocado, banana, breadfruit, fig, guava, lemon, lime, lychee, mango, papaya, pineapple, soursop, strawberry, and watermelon; and the recipes number in the hundreds. The nutritive value of each fruit is given, a bit of botany is included along with some excellent botanical prints, and there appears to be a lot of good eating to anticipate. For those who wish to vary their diet around a botanical theme, this is a book to be recommended.

C. P. SWANSON

GARDEN STATE. *The Story of Agriculture in New Jersey.*

By John T. Cunningham. Rutgers University Press, New Brunswick. $5.00. 288 pp.; ill. 1955.

WHERE THERE IS VISION. *The New Jersey Agricultural Experiment Station, 1880–1955.*

By Ingrid Nelson Waller. Rutgers University Press, New Brunswick. $5.00. xii + 284 pp. + 16 pl. 1955.

Despite their disparate titles, these two books have a common theme—the agriculture of the state of New Jersey. Although small in size (45th in the nation) and generally thought of as a highly industrialized, thickly settled state, New Jersey has a greater income per acre of farm land than any other state in the union. This is, of course, an understandable situation, for its farm products, raised intensively under the most modern conditions, are routed directly into the great cities of the East. The question of farm subsidies does not concern New Jersey agriculture to any extent because of the diversity of foods, and because of the relatively small size of its farms, which average about 70 acres.

In discussing his topic, J. T. Cunningham is principally concerned with the farm products of his state, and he gives an excellent account of the diversity, methods, and income of the state's 25,000 farms. Miss Waller, on the other hand, approaches her subject through the institution—the New Jersey Agricultural Experiment Station—and the men who have brought New Jersey's agriculture to its present productive state. The result is a eulogy, and apparently a well-deserved one, for as a type of institution more often than not characterized by mediocrity, Rutgers, as it is familiarly known, has had a notable success in its 75 years of existence. Selman Waksman, Nobel laureate in Physiology and Medicine, is probably better known than

any other member of the experiment station, but the complexity of agriculture is such as to demand competent specialists in a variety of disciplines. Fortunately, the success of Rutgers is not New Jersey's alone, and the discovery of streptomycin is but one example of its scientific wealth that has benefited all states and all nations. Ingrid Waller, having her own share of vision, has handled her subject ably, concisely, and with perception.

C. P. SWANSON

GENERAL AND SYSTEMATIC ZOOLOGY

THE POLYCHAETE FAUNA OF THE GOLD COAST. *Bull. Brit. Mus. (nat. Hist.), Lond., Zool., Vol. 3, No. 2.*

By Norman Tebble. The British Museum (Natural History), London. £1. 0s (paper). Pp. 59–148; ill. 1955.

Besides its taxonomic value, this report is of general interest as containing a key to the families of polychaetous annelids.

A HISTORY OF THE CLASSIFICATION OF THE PHYLUM BRACHIOPODA.

By Helen Marguerite Muir-Wood. The British Museum (Natural History), London. £1. 0s. viii + 124 pp.; ill. 1955.

The author is a student of fossil Brachiopoda and as such is perhaps naturally interested in the historical aspects of the group. The book attempts "to piece together the history of the phylum since 1758." Some old figures from pre-Linnaean days are reproduced in the study, and there is a discussion of early ideas as to the affinities of the Brachiopoda. Linnaeus included them in his miscellaneous group of Vermes Testacea and Cuvier in 1798 assigned them to the Mollusques Acephales, which besides bivalves, also included ascidians and barnacles. However, Cuvier soon realized the necessity of separating brachiopods from molluscan bivalves, and eventually he proposed the name "brachiopodes" as a class of Mollusca (1817). The form Brachiopoda is stated to have originated with Dumeril (1806), who took it from earlier works of Cuvier. Milne Edwards in 1843 proposed the unfortunate association of bryozoans and tunicates under the name Molluscoides, and Huxley (1853) proposed to include the Brachiopoda in this assemblage. This arrangement was adopted by some authors, while others continued to regard brachiopods as mollusks. Tunicates appear to have been dropped from the assemblage about 1870, and there followed a period of argument as to whether brachiopods are more nearly related to mollusks or to annelids. The name Tentaculata was proposed by Hatschek (1888) for the three groups Phoronida, Bryozoa Ectoprocta, and Brachiopoda; and this arrangement has met with recurrent favor, and appears in the *Handbuch der Zoologie* where, however, it is placed under Bütschli's Oligomera, a concept that in my opinion is totally false and artificial. Some zoological works still retain the name Molluscoidea for the same assemblage included under the Tentaculata, but most present opinion inclines to regard the Brachiopoda as a distinct phylum.

The second chapter of the publication is devoted to a discussion of the history of classificatory arrangements within the Brachiopoda, and the third chapter discusses present classifications. Muir-Wood accepts the division of the phylum into the classes Inarticulata and Articulata, and does not discuss Percival's suggestion to raise each of these classes to the rank of phylum. The classification presented is not intended as definitive but rather as a record of views in progress, and useful for purposes of reference. An extensive bibliography adds to the value of the book.

L. H. HYMAN

A HISTORICAL REVIEW OF THE MOLLUSKS OF LINNAEUS. *Part 3. The Genera Bulla and Voluta of the Class Gastropoda. Bull. Amer. Mus. nat. Hist., Vol. 107, Art. 1.*

By Henry Dodge. American Museum of Natural History, New York. $2.00 (paper). 157 pp. 1955.

The Linnaean genera *Bulla* and *Voluta* contained originally 23 and 48 species, respectively, but of these only 1 and 3 respectively remain today where Linnaeus placed them. Furthermore, although these genera are not now considered very closely related (they belong in different orders) and do not resemble each other very closely, there is a surprisingly large block of species which were assigned to *Bulla* in the tenth edition of the *Systema Naturae*, and then transferred to *Voluta* in the twelfth edition.

The old genus *Voluta* is now broken up into several different families, which constitute a compact group characterized by a plaited columella. Linnaeus attached great importance to these plaits and so assigned to the genus 2 species with plaited shells which are now placed in another order distinct from the first two, and in the genus *Ellobium*. They have been given the specific names *E. auris-midae* and *E. auris-iudae*. The first of these of course refers to the well-known character in Greek mythology who had ass's ears, but if there is any tale in classical folk-lore connected with the ears of Judas the reviewer would like to know what it is.

The old genus *Bulla* has likewise been dismembered, the species of which it was formerly composed now being dispersed among the families Strombidae, Tonnidae, Amphiperatidae, Muricidae, Turridae, and even the freshwater Physidae and the terrestrial Achatinidae. Apparently Linnaeus considered his genus as a sort of

home for incurables to which he consigned everything for which he could not find a place anywhere else.

The development of scientific thought is a legitimate field of investigation in its own right. To those who are interested in the history of malacology the series of which this volume is the third cannot be recommended too highly as a starting point.

Each of the three volumes which have so far been issued contains an index of the Linnaean names appearing in it. It is to be hoped that when the series has been completed the final volume will contain an index of all taxonomic names, Linnaean or otherwise, that have been mentioned in the entire series.

JOSHUA L. BAILY, JR.

MARINE MOLLUSKS COLLECTED DURING THE "ASKOY" EXPEDITION TO PANAMA, COLOMBIA, AND ECUADOR IN 1941. *Bull Amer. Mus. nat. Hist., Vol. 107, Art. 2.*

By Leo George Hertlein and A. M. Strong. American Museum of Natural History, New York. $2.00 (paper). Pp. 159–318 + 3 pl. 1955.

During the past quarter century a great impetus has been given to the study of Pacific Latin-American malacology, not only by the many scientific expeditions sent into this area by institutions that have discovered it anew, but also by many amateurs who have begun to take their vacations there as well. Despite a great demand for adequate textbook coverage the literature of this subject has never been integrated; some day it will be, and when that day comes one of the most important sources of data will be the various publications of Hertlein and Strong.

The present work is a report of a scientific expedition into Panamá, Colombia, and Ecuador, made in 1941. This was apparently undertaken for some purpose to which the gathering of molluscan material was more or less incidental, since the number of species taken is rather smaller than one would expect, and these for the most part have fairly large and conspicuous shells, such minute forms as the Pyramidellidae and *Rissoea* being entirely absent.

Only two new species are described in this publication, but many are reported for only the second time. The type locality of some of these lies outside the area visited by this expedition, so that each record constitutes an extension of range. Some of these record occurrences several hundred miles from the type localities, from which fact the value of this report to those engaged in faunistic work may be realized. There are, however, two instances of species which extend far beyond the ranges cited by Hertlein and Strong, who report the northerly range limits of *Murex radius* and *Murex erythrostomus* as Acapulco and Punta Peñasco, respectively, although I have myself taken a typical specimen of the former at Guaymas and had the privilege of examining two typical specimens of the latter that had been picked up on the beach at Ensenada de Todos Santos after a severe storm in 1897.

From the object of binomial nomenclature it follows that genera should be construed with sufficient breadth to give each genus at least one species that is widespread geographically, or at least one that is well known for some other reason. Some modern taxonomists have adopted the practice of splitting their genera so minutely that these cease to have very much meaning. The logical end of such procedure would be to give each species a genus to itself. The authors of the present work have construed their genera so broadly as to give them utilitarian value. For this they deserve thanks and congratulations. The extensive bibliography of about 500 items will be found most helpful.

JOSHUA L. BAILY, JR.

THE BUTTERFLIES OF SOUTHERN AFRICA. *Part II. Nymphalidae: Danainae and Satyrinae.*

By G. Van Son. Transvaal Museum, Pretoria, South Africa. £3 3s. x + 166 pp. + 37 pl.; text ill. 1955.

This is the second volume to appear of *The Butterflies of Southern Africa*, a study which will eventually cover the entire butterfly fauna of the region. Although interest in the subject will be restricted to specialists and to persons particularly interested in the butterflies of the area, this volume is recommended as a fine example of a regional butterfly book. The plates are particularly noteworthy. All are in color and beautifully reproduced. Considerable attention is given to life histories, both in the text and figures.

V. G. DETHIER

HANDBOOK OF MAMMALS OF KANSAS. *Contribution from the State Biological Survey of Kansas. Univ. Kans. Mus. nat. Hist., misc. Pub., No. 7.*

By E. Raymond Hall. Museum of Natural History, University of Kansas, Lawrence. Free upon request (paper.) 303 pp.; ill. 1955.

The technical portion of the text of this book is essentially a republication of Cockrum's volume of similar title published in 1952, and now out of print. A few new distribution records have been added to bring the information up to date.

To the technical synopses the present author has added semitechnical accounts primarily for the delectation of the lay reader. The book is handsomely prepared and should find as wide an acceptance among Kansas naturalists as have all previous publications on this subject.

BRYAN P. GLASS

LES MAMMIFÈRES DE L'AFRIQUE NOIRE FRANÇAISE. *Initiations Africaines, I. Second Edition.*

By P. L. Dekeyser. Institut Français d'Afrique Noire, Dakar. 1,200 fr. (paper). 426 pp.; ill. 1955.

The arrangement of this book suggests that it might be designated as an annotated check-list. The first part is devoted to a general discussion of the morphology and biology of mammals. The most interesting part to those reading it for information particularly concerning the African fauna will be the section on the biogeographic zones. The author recognized the Palaearctic region, consisting of the Sahara and the north coast. South of this, he recognizes the Ethiopian as being divided into two subregions, the western and eastern. The former includes the Guinea Coast and the Congo basin, the latter the entire remainder of the continent. The area discussed in this book falls largely in the western subregion, and includes the Guinea savannas and the Guinea and Congo forests, while the northernmost part includes the western Sudanese part of the so-called eastern subregion.

The second part, comprising the greater portion of the book, is devoted to a systematic synopsis of the mammalian fauna of the region. The larger families are provided with dichotomous keys for identification of genera. Not all groups are treated equally. For instance the bats receive only brief mention, closing with a short section on the biology of the order. Most other groups not only have a systematic synopsis, but are discussed by species as well as to their habits, parasites, distribution, etc. Rodents receive fair treatment, and the larger mammals, especially the large carnivores and big game, are for the most part generously favored.

The author is a gifted artist, judging by the excellent and lifelike pen-and-ink sketches with which the text is liberally illustrated. A useful appendix cites the species of parasites known from the mammals of the region. They are listed phylogenetically, followed by a list of known hosts.

BRYAN P. GLASS

LIVING MAMMALS OF THE WORLD.

By Ivan T. Sanderson; photographs by John Markham, Roy Pinney, Cy La Tour, Ylla-Van Nostrand, Ernest P. Walker, and others. Hanover House, Garden City. $9.95. 303 pp.; ill. No date.

The author needs no introduction as a gifted lecturer and writer on subjects dealing with natural history, but in this volume he has outdone himself in producing a minor classic exciting to read, informative without being overwhelming in its use of technical terminology, and truly exceptional in the sheer beauty and artistry of its 330 photographs. Nearly 200 of these are in full color, and are a living tribute to the many photographers who have generously contributed to this volume.

The scope of Sanderson's book is world-wide, and is divided into familial rather than geographical groupings. The text is written with a minimum of zoological jargon, yet covers the essential points of taxonomic, ecologic, and geographic differences as well as many facets of natural history. It does in book form what Walt Disney has done through the medium of motion pictures, and does it equally well. It is a book recommended to all, from the casual reader to the specialist; it cannot help but inform and delight.

C. P. SWANSON

ANIMAL GROWTH AND DEVELOPMENT

EMBRYOLOGIE. *Ein Lehrbuch auf allgemein biologischer Grundlage.*

By Dietrich Starck. Georg Theime Verlag, Stuttgart. DM 78.—; $18.55. xx + 688 pp.; ill. 1955.

It is in some ways a most astonishing fact, in the light of recent non-biological history, that the truly comprehensive books on embryology which are appearing in the 1950's are being issued from publishing houses of the Old rather than of the New World. Without entering here into possible explanations for this situation, it suffices to point out that now that Dietrich Starck's *Embryologie* has joined Kühn's *Entwicklungsphysiologie*, Tome XII of the *Traité de Zoologie* devoted to comparative embryology, and Waddington's *Principles of Embryology* on the embryologists' bookshelves. A group of excellent texts, each of which is supplementary to the others, has been assembled within the space of a very few years, and finds no counterpart contributed by authors on this side of the Atlantic. Two of the volumes just mentioned have been reviewed recently in these columns, and notice of Waddington's will appear in them shortly. The present review will confine itself to a few comments on Starck's book.

This describes itself as a textbook based on the foundations of general biology, and it could hardly be more aptly characterized. Its first general part (Conditions of Development, and the Construction of the Vertebrate Body) takes up (1) the germ cells, fertilization, the chromosome theory of inheritance, sex determination, and sexuality; (2) cleavage; (3) gastrulation and embryo formation in holoblasts; (4) early development in meroblasts; (5) the first origins of blood and the vascular system; (6) the early development of mammals; and finally, a few pages on functional adaptation in development and on post-embryonic development. The special part, which concentrates on the development of organ-systems, discusses in turn (1) the nervous system and sense organs; (2) the gut, respiratory organs, and coelome; (3) the urinogenital system; (4) the circulatory organs; and (5) the skeletal system and musculature. A short section on the problem of the

vertebrate head concludes the second part. Three appendices deal with the classification of vertebrates and include various data concerning the number and size of the young and the length of their period of development or gestation. The illustrations, many of them original photographs, are excellent, and there is an extensive and up-to-date bibliography.

This is not the first recent attempt in the German language to base a comprehensive understanding of vertebrate morphogenesis on the broad foundations of general biological and experimental investigations. Brandt in 1949 and Goerttler in 1950 have made previous abortive efforts in the same direction. Starck, however, has gone far beyond them both. His treatment is more inclusive and more mature. He has a clear command of a vast array of facts, and also the ability to express himself lucidly and succinctly. He has, furthermore, considerable felicity of style, and his book reads like a novel. Except for some rather spongy and turgid passages concerning the placenta, the writing is fast, graceful, and fluid.

The author, furthermore, permits himself to express a number of independent and individual ideas of his own. For one example, he questions the validity of classifying the mesencephalon as a primary brain vesicle. Starck would consider both tegmentum and tectum to represent part of the rhombencephalon; and he would hold that the large optic tectum of the chick, so frequently studied, misled embryologists to place their conventional emphasis on the mesencephalon as a primary vesicle. This is not the only example in the book where the attempt is made to elucidate the conditions in mammals by what is known of the birds, or of other vertebrates, or even of invertebrates—in fact, the concept of induction is introduced by a discussion of echinoderm, and not vertebrate, development. The reliance of the author on both facts and concepts derived from the knowledge of the widest possible sources of material has enabled him to achieve his aim of presenting embryology on a broad biological basis, and his volume is therefore strongly to be recommended to all contemporary students and investigators of development.

JANE OPPENHEIMER

THE GROWTH-STAGES OF THE POUCH-YOUNG OF THE NATIVE CAT (*DASYURUS VIVERINUS*) TOGETHER WITH OBSERVATIONS ON THE ANATOMY OF THE NEW-BORN YOUNG. *Trans. zool. Soc. Lond., Vol. 28, Part 5.*

By the late J. P. Hill, and W. C. Osman Hill. £2 15s. (paper). Pp. 349–452 + 13 pl. 1955.

Several things strike the reader of this paper and make him envious of the authors. First of all, they have chosen a subject that is of wide interest to both mammalogists and students of development. Even more unusual is the notation that the material was collected on a grant during the years 1895 to 1905! At a time when one is expected to produce a publication within a year or two after a grant has been received, this is indeed refreshing. Still another basis for envying the authors is the manner in which the work is published, the excellence of the illustrations, the care with which the printing has been done, and the fact that the authors were permitted 76 pages of text and 13 plates with 60 figures in this day, when journals are apparently unwilling to publish more than a few pages and a few plates.

The quality of the work is worthy of the style in which it is published. It is divided into two parts, the first and shorter part being on the growth stages of the pouch young. This section includes, in addition to the introductory discussion of the marsupial pouch and the migration of the new-born young into it, a consideration of the nursing period and the manner of nursing. There is a good discussion of the theories of the role of the cremaster muscle as a mammary compressor. The section ends with a discussion of the ageing of early stages and a systematic description of the stages and finally a discussion of the growth of the pouch young. The second section is on the anatomy of the new-born young. Yet within this section are included such topics as the length of gestation, the adaptive nature of some structural features as well as the function of these structures and the description of the anatomy. Both sections are very well done and are so written as to be of use and interest to any intelligent reader. This is not to say that much of the anatomical detail might not be skipped over by most readers: what remains is still clear and stimulating to a non-professional person.

The authors show not only great familiarity with the material with which they have worked, but they have obviously worked on many species of marsupials. In addition to this, they are familiar with the literature on the group. This familiarity has enabled the authors to publish a paper that is complete and that will stand as the classic writing on the subject for some time to come.

ROBERT K. ENDERS

MOLECULAR EVENTS IN DIFFERENTIATION RELATED TO SPECIFICITY OF CELL TYPE. *Ann. N. Y. Acad. Sci., Vol. 60, Art. 7.*

Edited by Roy Waldo Miner; 17 contributors. New York Academy of Sciences, New York. $3.50 (paper). Pp. 965–1160; ill. 1955.

Four papers constituting the first section of this symposium deal with Patterns of Synthesis in Differentiation. They were prepared by Louis B. Flexner, Clement L. Markert, Charles E. Wilde, Jr., and James D. Ebert and colleagues. The second part includes contributions by Ernst Caspari, George W. Nace, Melvin Spiegel, and by A. M. Schechtman and T. Nishihara. In the

final portion, entitled Problems of Structural Organization, the articles are by Clifford Grobstein, Alexander G. Karczmar, and S. Meryl Rose. The quality of the individual contributions is highly disparate. Most of them present fairly detailed reports on the current status of the rather specialized investigations of the individual authors, the immediate relevance of which to the very general topic supposedly under coverage is not always apparent. Presumably the papers encouraged some fruitful discussion at the actual symposium, which was held in October 1954. To the reader, they serve as adequate surveys of work up to 1954, until such time as they are superseded, as some have been already, by more recent and more thoughtfully comprehensive reviews.

JANE OPPENHEIMER

ANIMAL MORPHOLOGY

VERGLEICHENDE ANATOMIE UND MORPHOLOGIE DER WIRBELTIERE. *I. Lieferung.*

By W. Marinelli and A. Strenger. Franz Deuticke, Wien. DM 30.—(cloth); DM 27.—(paper). 80 pp.; ill. 1954.

The first volume of this work on comparative vertebrate anatomy is announced to comprise 12 chapters, each of which will consist of an illustrated descriptive account of a vertebrate type. The present chapter (Lieferung) is devoted to the European lamprey, *Lampetra fluviatilis*, and is abundantly illustrated with fresh drawings made from the dissections. The series should be of value to students of vertebrate anatomy.

L. H. HYMAN

ANIMAL PHYSIOLOGY

ÉQUILIBRES ET DÉSÉQUILIBRES BIOLOGIQUES. *Sensibilité Organique et Méthodes Thérapeutiques.*

By Maurice Vernet. G. Doin & Cie., Paris. 1,200 fr. (paper). 278 pp. 1954.

The history of progress in medicine (and more particularly in physiology) has been directly related to the progress of our understanding of the integrated functioning of the organism as a whole, and of its equilibrium with the internal and external environment. These problems have intrigued and been the focus of the efforts of many of the most outstanding investigators. Certainly anyone working in any field of experimental biology and medicine is aware of the contributions in this regard of, for example, Claude Bernard and Walter Cannon.

As a result of such interest and innumerable brilliant studies, we have come to understand how many bodily features are automatically maintained in a state of equilibrium. Every aspect of the internal environment is subject to regulation directed toward keeping it in a steady state. There are mechanisms for maintaining constant temperature, constancy of water content of the blood, of salt content of the blood, blood sugar, proteins, fat, calcium, etc. Homeostatic mechanisms ensure an adequate supply of oxygen to the cells as well as maintain other protective cycles. Most recently we have begun to investigate and understand the equilibratory mechanisms associated with emotional disturbance or stress, and the loss of equilibria which leads to what is now being termed psychosomatic disease.

Vernet's book has as its primary goal the emphasis upon and clarification of the basic role of the nervous system in the production and maintenance of the biological equilibria which are essential to the life of the organism. It follows two previous works, *La Sensibilité Organique* and *La Vie et la Mort*. Based essentially on physiology, it examines the equilibria and shifts from them, which affect the normal, functional state of the organism. The second part of the book is devoted to the mechanisms at work in the rhythmic functional cycles of health and illness: cellular equilibria, nutritional and respiratory equilibria, endocrine equilibria, and thermal and cardiovascular steady states. The third section deals with the loss of equilibria and consequent loss of adaptation, regulation, and organismic defenses. The last section of the book discusses losses of mental equilibria, i.e., psychosomatic organismic vertigo.

The author covers a wide field, necessitating certain integrations of physico-chemical, biological, and philosophical concepts. In the present state of our knowledge this sort of effort is almost bound to result in the production of something akin to Jacob's coat—and so it has. Nonetheless, whether or not we agree with this or that idea or synthesis, it is enormously fascinating to think as Vernet has done, in terms of trying to make sense out of such a hodge-podge of tantalizing observations and suggestions. By seriously attempting such an analysis and synthesis of general biological, physiological, clinical, therapeutic, and philosophical ideas and mechanisms, he has done us all a service, whether or not we care to agree with everything he has to say. The work could be considerably improved by an adequate and accurate bibliography.

R. G. GRENELL

TEXTBOOK OF PHYSIOLOGY. *Twelfth Edition.*

By William D. Zoethout and W. W. Tuttle. The C. V. Mosby Company, St. Louis. $5.25. 703 pp. + 5 pl; text ill. 1955.

"The mixture as before," but somewhat rearrangp9 (for the better) and expanded over previous editions to give more emphasis to biochemical aspects of physiology.

CLAUDE F. BAXTER

RÉSISTANCE ET SOUMISSION EN PHYSIO-BIOLOGIE. *L'Hibernation Artificielle. Collection: Évolution des Sciences, 2.*

By H. Laborit. Masson & Cie., Paris. 650 fr. (paper). vi + 120 pp.; ill. 1954.

Among the more startling procedures of modern surgery are those carried out during the temporary interruption of the blood flow to essential organs. For example, occlusion of the carotid arteries to permit replacement of large segments of the aortic arch is now possible through the use of hypothermia and certain other measures. A considerable impetus to the application of hypothermia was given by Laborit, who with Huguenard concocted the famous "lytic cocktail." This monograph is a summary of Laborit's working hypotheses and concepts; it is primarily a popularization rather than a conventional exposition of data and results.

Exceptions are taken to what may have been considered solidly entrenched concepts. Claude Bernard's dictum on the internal environment is complemented by the suggestion that the constancy of the intensity of vital processes is maintained rather than the constancy of composition. It is also suggested that so-called "defense mechanisms" are reactions to "aggression" and are better suited to facilitate the escape of the free subject from the environmental stresses than to preserve all vital functions. As an example, Laborit mentions the maintenance of peripheral arterial pressure in hemorrhage at the cost of renal ischemia and the eventual production of acute renal insufficiency. There follow considerations of the roles and interrelationships of ganglionic blocking agents, of anterior pituitary and adrenal hormones, and of hypothermia in affecting specific body reactions to different stresses or situations. Among the latter are prematurity and old age, hemorrhage and shock, toxic agents and infections, and surgical procedures. The importance of agents such as chlorpromazine in potentiating the effects of barbiturates and of hypothermia are emphasized. Laborit's main thesis is that his technique suppresses the "defense mechanisms" and allows the organism to submit to the environment imposed on it. Of considerable practical importance in the field of surgery, this work and these concepts should also be of general interest to physiologists and other biologists.

F. P. CHINARD

THE KIDNEY. *Ciba Foundation Symposium arranged jointly with the Renal Association.*

Editor for the Renal Association, A. A. G. Lewis; editor for the Ciba Foundation, G. E. W. Wolstenholme assisted by Joan Etherington. Little, Brown & Company, Boston. $6.75. xvi + 333 pp.; ill. 1954.

This book embodies a verbatim account of the proceedings at an international conference on the kidney held in London in July, 1953. Twenty papers were presented, under the following general headings: Structural and Functional Relationships in the Kidney; Tubular Functions other than the Regulation of Acid-Base Balance; Renal Share in the Regulation of Acid-Base Balance; General Problems of Electrolyte Excretion; and Renal Share in Volume Control of Body Fluid. The resulting volume can be highly recommended as a stimulating and critical survey of major problems in the physiology of the kidney, and in the applications of physiological considerations to the clinical management of renal disorders.

EVELYN HOWARD

THE COMPARATIVE ENDOCRINOLOGY OF VERTEBRATES, PART I. THE COMPARATIVE PHYSIOLOGY OF REPRODUCTION AND THE EFFECTS OF SEX HORMONES IN VERTEBRATES. *Mem. Soc. Endocrinol., No. 4.*

Edited by I. Chester Jones and P. Eckstein. Cambridge University Press, New York. $8.50. x + 253 pp. + 10 pl.; text ill. 1955.

This memoir is Part I of a projected series on the comparative endocrinology of vertebrates, and comprises the proceedings of a symposium held in July, 1954, at the Department of Zoology in the University of Liverpool. The symposium ranged over a very wide field, with the aim of constructing an up-to-date picture of the comparative endocrinology of the vertebrates, as well as attempting to put old biological problems into the perspective of modern endocrinological concepts, and, at the same time, to relate newer ideas in endocrinology to the facts of zoology. Discussions were presented on Reproduction in Teleosts (W. S. Hoar); Amphibia (G. J. and P. G. W. J. Van Oordt, and C. L. Smith); Reptilia (R. Kehl and C. Combescot); Birds (A. J. Marshall and W. R. Breneman); Mammals (S. Zuckerman and P. Eckstein); The Evolution of Viviparity in Vertebrates (L. H. Mathews); Vertebrate Gonadotrophins (E. Witschi); Sex Hormones in Fish and Lower Chordates (J. M. Dodd); Sex Development in Amphibia (L. Gallien); Sex Hormones in Birds (R. M. Fraps); Effects of Sex Hormones in Mammals (J. H. Leathem and R. C. Wolf); and Modalities in the Actions of Gonadal and Gonad-stimulating Hormones in the Foetus (A. Jost). Comments from the audience are recorded; there are bibliographies, and graceful closing remarks by S. Zuckerman, the chairman.

The memoirs contain much interesting material, and the conference is to be commended for directing attention to an important field which is relatively undeveloped. The papers were rather uneven in quality, some being rather successful in presenting surveys with a good deal of perspective, or in pointing up a few significant observations, while others were rather tightly packed with minutiae. In general, the papers give the impression that in spite of much beautiful work, there

is no dearth of opportunity to contribute to a deeper understanding of the evolution of steroid hormone regulation of biological activities.

EVELYN HOWARD

THE COMPARATIVE ENDOCRINOLOGY OF VERTEBRATES. PART II. THE HORMONAL CONTROL OF WATER AND SALT-ELECTROLYTE METABOLISM IN VERTEBRATES. *Mem. Soc. Endocrinol., No. 5.*

Edited by I. Chester Jones and P. Eckstein. Cambridge University Press, New York. $4.75. x + 124 + ii pp.; ill. 1956.

In this conference held under the chairmanship of S. J. Folley, the central theme is the role of the posterior pituitary and of the adrenal cortex in the distribution and passage of water and certain ions across biological barriers. The contributions are by active investigators in each particular field and contain not only summaries of previous work but also accounts of unpublished work in progress. Each contribution is followed by discussions by one or more of the participants in the conference. In the first paper, E. J. Conway reviews the hormonal control of water, sodium, chloride, and potassium metabolism in muscle and yeast cells, and discusses briefly the applicability of the "redox pump" theory to these systems. The second paper, by H. Heller, is on the secretory control of the neurohypophysis in higher vertebrates. W. H. Sawyer reviews water and salt metabolism in amphibia, with emphasis on the frog's kidney. Frog skin and the effects of the posterior pituitary on its properties are next discussed by V. Capraro and M. L. Garampi. M. Fontaine follows with a very clear and succinct exposition of water and electrolyte metabolism in fish. This is complemented by D. C. W. Smith's paper on the role of endocrine organs in the salinity tolerance of trout. The concluding paper, by I. Chester Jones, is on the effects of adrenalectomy and of steroids on salt and water metabolism in such experimental subjects as the opossum, trout and other fishes, and various reptiles.

This volume will be of considerable interest to biologists and to physiologists not only as a convenient source of information but also as a stimulus to further work. Much information is available about the factors which influence salt and water metabolism; little information is available at present about the mechanisms.

F. P. CHINARD

THE THYROID. *Brookhaven Symp. Biol., No. 7.*

Brookhaven National Laboratory, Biology Department, Upton, N. Y.; Office of Technical Service, Department of Commerce, Washington. $1.75 (paper). viii + 271 pp.; ill. 1955.

This book is a report on the seventh annual symposium held by the Biology Department of Brookhaven National Laboratory, June 9–11, 1954. This symposium was an attempt to collate and discuss the many recent advances, new hypotheses, and new concepts in thyroid physiology. The program was very successful in achieving this goal. All of the articles are very concise and informative. The articles on the phylogenetic and developmental aspects of the thyroid, by A. Gorbman, and on spontaneous hyperplasia and neoplasia of the thyroid, by H. G. Schlumberger, are of great interest to the zoologist. Other articles, like S. B. Barker's essay on the circulating thyroid hormone and by A. Taurog on the conjugation and excretion of the hormone, will appeal to the biochemist. E. B. Astwood gives a masterly review of the mechanism of action of antithyroid compounds. He states that "a review of the data concerning the action of antithyroid compounds has led to the conclusion that these compounds act by interfering with the conversion of iodide to iodine, and that the enzyme system responsible for this conversion is a peroxidase." Comments and discussions are reported verbatim after each paper. These remarks are most stimulating; the reader will find excellent suggestions and information here. At the conclusion of each article a list of pertinent references is given. The book is well illustrated. An author index and a subject index greatly enhance the value of the book as a reference work. The price is most reasonable, so that the purchase of this volume can be recommended to every biologist and clinician.

W. FLEISCHMANN

THE THYROID GLAND. *Mem. of the Soc. for Endocrinol. No. 1. Proceedings of a Symposium held jointly by the Soc. for Endocrinol. and the Endocrinol. Section of the Royal Soc. of Med., at the Royal Soc. of Med., London, February 25, 1953.*

Edited by P. Eckstein and S. Zuckerman. Cambridge University Press, New York. $2.00. 48 pp. + 4 pl.; text ill. 1955.

The papers in this brief publication are of great interest both to the physiologist and to the clinician. The latter will find the article on the diagnostic value of serum protein-bound iodine estimation very helpful in evaluating results obtained by this difficult chemical procedure. R. R. de Mowbray and A. Tickner from Guy's Hospital (London) come to the conclusion that the estimation of serum protein-bound iodine levels is valuable chiefly in the clinical diagnosis of thyroid disorders in infants and young children, in elderly subjects or in the presence of cardiac, respiratory, neurological, and mental disease, particularly where hypothyroidism is suspected. The fact that the serum protein-bound iodine level is not consistently raised in cases of hyperthyroidism is considered a disadvantage of the method. An article by S. L. Hignett on thyroid histology in cattle enhances our knowledge of comparative endocrinology and is excellently illustrated

Rosalind Pitt-Rivers, who has contributed so much to recent developments in the biochemistry of the thyroid, reports on the physiological activity of triiodothyronine. Sir Charles Harington, in his opening remarks, shows how the recent advances in thyroid physiology depend on the interplay of ideas from various sources and on the employment of a multiplicity of techniques. Pertinent references are given and the general discussion is abstracted briefly. The book is valuable because it gives us access to the thoughts of the foremost English and French investigators of thyroid function.

W. FLEISCHMANN

LES ANTITHYROIDIENS BIOLOGIQUES.

By J. Cosma; preface by P. Rohmer. G. Doin & Cie., Paris. 1,500 fr. (paper). 200 + ii pp.; ill. 1953.

The author here attempts to bring together all information available on physiological regulators of thyroid function and on the antithyroid compounds. Reference is made to 1476 publications, which are listed in the bibliography. A great wealth of facts is presented, but the discussion is far from critical. As an annotated bibliography of certain aspects of the physiology and pathology of the thyroid gland this monograph should be useful to the specialist.

W. FLEISCHMANN

CIBA FOUNDATION COLLOQUIA ON ENDOCRINOLOGY. *Volume VIII. The Human Adrenal Cortex.*

Edited by G. E. W. Wolstenholme and Margaret Cameron; assisted by Joan Etherington. Little, Brown & Company, Boston. $10.00. xvi + 665 pp. + 42 pl.; text ill. 1955.

This is an important source of information regarding current research in a very active field. The volume consists of 36 papers and the discussions at two conferences held in London in April and June, 1954, under the auspices of the Ciba Foundation. The work reported was by no means limited to studies in human subjects. The first conference was concerned mainly with histological and biochemical aspects and with corticomedullary relationships, under the chairmanship of Gregory Pincus. The second conference dealt with the clinical physiology and pathology of adrenal function, and with hypothalamic and pituitary relationships considered at various levels, including the psychiatric. George Thorn, in opening the second conference, remarked that "the first seventy five years of the past century, speaking chronologically from the adrenal viewpoint, were devoted to the unravelling of the distinctive features and functions of the cortex and medulla. The future will undoubtedly be concerned with putting them back together again. . . . Although we, as clinical investigators, may be proud of the progress which has been made in the field of adrenal cortical function, we are humble indeed in our appreciation of what the future conceals."

EVELYN HOWARD

VITAMINS AND HORMONES. *Advances in Research and Application. Volume XIII.*

Edited by Robert S. Harris, G. F. Marrian, and Kenneth V. Thimann. Academic Press, New York. $9.00. xii + 382 pp.; ill. 1955.

The thirteenth volume of this series consists of review articles of 9 subjects. The chapter on the role of the vitamins in antibody production, by A. E. Axelrod and J. Pruzansky, reviews the several dietary factors which may influence the susceptibility of a host to infection. A tabulation of 8 of the B-vitamins shows the ability of various species to form antibodies during vitamin deficiency. A closely related chapter on parasitic infections and nutrition is contributed by D. A. Smith. The late Harry J. Deuel and R. Reiser are authors of a chapter on the physiology and biochemistry of the essential fatty acids. They discuss the bioassay, comparative potencies, interconversions, and factors affecting the requirement for essential fatty acids. A discussion of the biosynthesis of ascorbic acid, by L. W. Mapson, covers various phases of the problem from the mechanism of conversion from hexose sugars to the dependence of biosynthesis on external factors in plants and animals. Other chapters on vitamins are as follows: The Role of B_{12} in the Metabolism of Microorganisms (J. E. Ford and S. R. Hutner); The Chemotherapeutic Action of Vitamin B_{12} (C. C. Ungley); and The Vitamin Requirements of Human Beings (L. B. Pett). The two final papers are concerned with the action of hormones. W. S. Bullough covers the energy requirements in mitosis and the influence of hormones on carbohydrate metabolism and mitosis. He discusses the interesting observation that the naturally occurring mammalian estrogens stimulate the glucokinase system. O. Hechter presents the controversial subject of possible mechanisms of hormone action by presenting current answers to two questions, (1) how can trace amounts of hormones produce profound biological effects in target cells without contributing either significant amounts of energy or matter to the system? and (2) how can the specificity of hormone action be accounted for?

The volume is another outstanding contribution and should be of considerable value to workers in various fields of biology and medicine.

R. VAN REEN

NUROLOGY. *Volumes 1, 2, and 3. Second Edition.*

By S. A. Kinnier Wilson; edited by A. Ninian Bruce. The Williams & Wilkins Company, Baltimore. $37.50 (3 vols.). (1) xiv + 702 + 31 p. index; ill. (2) x +

703–1352 + 22 p. index + 2 pl.; text ill. (3) x + 1353–2060 + 99 p. index; ill. 1955.

To all who have in any way been concerned with the medical aspects of nervous system function, Wilson's *Neurology* has long been a classic reference. There is no need to describe it in detail, inasmuch as it has represented for many years a monument to the memory of a great clinician.

It is most unfortunate, however, since the need for a new edition was obvious, and extremely able people were willing to carry it out, that more effort was not expended in making it the sort of up-to-date, thorough, and modern text its author would presumably have liked it to be. Sometimes one is impressed with the failure of people to realize that great minds are the first to point out, see, and accept new trends and concepts. Such people would be chagrined to see how often sentimentality is responsible for the perpetuation of ideas they would long since have left behind if they had themselves had the opportunity to do so. In this instance, one feels that Kinnier Wilson would have wished a current edition of his book to have been radically changed so that it would be a really living and not so massive and moribund a memorial.

R. G. GRENELL

EXCITABILITÉ NEURO-MUSCULAIRE ET ÉQUILIBRE IONIQUE. *Intérêt Pratique en Chirurgie et en Hibernothérapie.*

By H. Laborit and G. Laborit. Masson & Cie., Paris. 880 fr. (paper). iv + 107 pp.; ill. 1955.

In this monograph the authors consider the problems of neuromuscular excitability and of ionic distribution between intracellular and extracellular phases of the body in their relationship to surgical procedures and to artificial hibernation.

A very brief review of membrane phenomena, particularly in relation to the effect of temperature changes on the distribution of calcium and potassium between intracellular and extracellular phases, is followed by a chapter on what is called cellular excitability. Use is made of the concept of chronaxie and the relationship between duration of stimulus and current intensity to obtain a measure of this cellular excitability and to correlate the latter with the ionic composition of blood. Data are presented bearing on the entry of potassium into cells after administration of such substances as chlorpromazine and meperidine and after artificial hibernation. The effects of phenothiazine and its derivatives are also considered. Emphasis is given to the decrease of catabolism occurring in hibernation upon the administration of these drugs, as representing a suppression of the body's defense mechanisms. A few comments and illustrative case reports are given on the application of these concepts to surgical cases and to the management of electrolyte changes.

The book is irritating in that too hypothetical a structure is built on an inadequate experimental basis. Yet the practical benefits are impressive. A very real advance has been made by these methods in the management of many surgical and some medical problems. Perhaps further more detailed investigations of the very complex reactions to artificial hibernation and to the use of the adjuvant drugs will be forthcoming to supplement the few data now available.

F. P. CHINARD

EXPERIMENTAL PHARMACODYNAMICS.

By T. Koppanyi and A. G. Karczmar. Burgess Publishing Company, Minneapolis. $5.00. (paper). xvii + 256 pp.; ill. 1955.

This is a laboratory manual for students of pharmacology. Its purpose is to develop a scientific background for the use of drugs in the prevention, diagnosis, and treatment of disease. There are 12 sections covering the usual branches of pharmacodynamics. Each experiment is tied to clinical applications which correlate theory with practice. The laboratory exercises are the outgrowth of the long experience of the authors as successful teachers of pharmacology. Many may wish to use this text in their teaching course in pharmacology.

C. JELLETT CARR

FAT METABOLISM. *A Symposium on the Clinical and Biochemical Aspects of Fat Utilization in Health and Disease.*

Edited by Victor A. Najjar. The Johns Hopkins Press, Baltimore. $4.50. viii + 185 pp.; ill. 1954.

The symposium published in this volume was held at the Johns Hopkins University School of Medicine, and consists of papers by a number of experts in the fields of medicine and biochemistry.

Following an introductory chapter on the clinical and biochemical features of fat metabolism, by V. A. Najjar, there is a series of papers on the subject of obesity. A discussion by H. H. Gordon on obesity in childhood is followed by a chapter on multiple causative factors in obesity by J. Mayer. Constitutional and endocrine factors in obesity are discussed by B. Childs and L. Wilkens, respectively. The current interest in problems related to overweight makes these discussions especially appropriate. While a considerable body of data is presented, one cannot help but agree with some of the authors that more investigations of the problem are essential before an integrated view of obesity and its causes can be made.

Four papers are concerned with the blood lipids. L. E. Holt discusses lipemia; and E. H. Ahrens, Jr., problems related to essential hyperlipemia. This is followed by a paper on the preparation, utilization, and

importance of neutral fat emulsions in intravenous alimentation, by H. C. Meng. C. B. Anfinsen contributes some exciting findings in regard to the role of the lipemia-clearing factor in lipid transport. He draws an analogy with the hormonal control of blood sugar in suggesting that a similar homeostatic mechanism may apply to lipids, but with the secretion of heparin as the controlling factor.

The final papers of the book are devoted in the main to biochemical studies on lipid metabolism. F. Lipmann discusses the role of coenzyme A in fat metabolism. The enzymatic oxidation and synthesis of fatty acids are covered by A. L. Lehninger. Other papers are: The Mechanism of Diabetes Mellitus (S. P. Bessman); Lipogenesis in Vitro and its Hormonal Control (S. Gurin); Lipid and Phospholipid Synthesis (A. Kornberg); and Some Aspects of Cholesterol Metabolism related to Atherosclerosis (R. G. Langdon).

The collection of papers represents an outstanding contribution to a field of considerable current interest and should be a valuable acquisition for physicians, biochemists, and nutritionists.

R. Van Reen

Actualités Pharmacologiques. *Huitième Série. Published under the direction of René Hazard; contributors, M. Beauvallet, G. Brouet, P. Duquénois, H. Hermann, A. Quevauviller, J. Salva, and M. Tausk. Masson & Cie., Paris.* 1,480 fr. (paper). iv + 196 + ii pp; ill. 1955.

In this, the eighth volume of this series, seven reviews on topics of current pharmacological interest are included. A general review of the effects of epinephrine and of nor-epinephrine, by Beauvallet, is complemented by a more detailed discussion, by Hermann, of adrenergic blocking agents and of the hypotension which results from the administration of adrenalin after an adrenergic blocking agent. The effects of acetaldehyde are also reviewed briefly. Synthetic agents effective in tuberculosis are described by Brouet. Duquénois has an interesting essay on antibiotic substances obtained from higher plants. Of little practical clinical interest at present, these substances have possibilities as agents against bacteria which are resistant to currently used antibiotics, and perhaps even against viruses. Other substances of plant origin, the Rauwolfia and Veratrum alkaloids, are discussed by Salva. Theophylline and its derivatives are reviewed by Quevauviller and vitamin B_{12} by Tausk.

These reviews are well organized and well written. Use is made of experimental data to illustrate particular points. The bibliographies are extensive and up to date. The contents should be of interest to physiologists, biologists, and clinicians as well as to pharmacologists.

F. P. Chinard

ANIMAL NUTRITION

Trace Elements in Human and Animal Nutrition. *By E. J. Underwood. Academic Press, New York.* $9.50. xii + 430 pp.; ill. 1956.

Although many specialized areas of nutrition and biochemistry have been adequately covered in recent books and reviews, no comprehensive consideration of the field of trace elements in human and animal nutrition has hitherto appeared. This volume is an attempt to fill part of this gap, and was written for specialists and students of nutrition. The biochemist may find the volume of general interest, but its emphasis is not on the mechanisms of action of the various elements but rather on the distribution and forms of the elements in tissues, absorption, excretion, deficiencies, requirements, and toxicity.

The trace elements discussed in considerable detail are iron, copper, molybdenum, cobalt, zinc, manganese, iodine, fluorine, and selenium. Briefer mention is made of nickel, aluminum, arsenic, barium, strontium, boron, bromine, silicon, and vanadium, since less is known about them and no known requirements have been established.

Ultimately man and other animals depend for their food upon plants, which in turn depend upon the soil for their supply of elements. The final chapter of the book is devoted to the interrelationships between these groups. The author clearly indicates that because of the difference in the mineral requirements of plants and animals, soil deficiencies may not result in poor plant growth although the animals grazing on such pastures suffer from deficiencies. Such relationships are of considerable interest and economic importance and should be more fully investigated. The book is well documented, with a bibliography following each chapter. The review of the subject matter is through 1954.

R. Van Reen

Vitamins in Theory & Practice. *Fourth Edition. By Leslie J. Harris. Cambridge University Press, New York.* $6.50. xxii + 366 pp.; ill. 1955.

This volume of *Vitamins in Theory and Practice* is a greatly expanded version of previous volumes. The author has not altered his basic aims, however, of emphasizing only the highlights of our present knowledge of nutrition in order to present an easily read and highly interesting story.

Each of the vitamins is covered in the text, including its discovery, the symptoms both gross and microscopic, of deficiency, and the sources of the vitamins in common foods.

All essentials for understanding the important problems in nutrition are presented in a manner that should appeal to those without much formal training in nutri-

tion and biochemistry but who have more than a passing interest in the field.

R. VAN REEN

THE REGULATION OF HUNGER AND APPETITE. *Ann. N. Y. Acad. Sci., Vol. 63, Art. 1.*

Edited by Roy Waldo Miner; 16 contributors. New York Academy of Sciences, New York. $3.00 (paper). Pp. 1–144; ill. 1955.

Another timely contribution by the New York Academy of Sciences, these 13 papers result from a conference held by the section of Biology on November 19–20, 1954.

The regulation of energy intake and body weight is discussed by Jean Mayer in terms of the glucostatic theory and the lipostatic hypothesis. While the glucostatic theory has considerable evidence in its favor, such as the correlation of the hunger sensation with a decrease in the arterial-venous (A-V) glucose difference, the influence of hormones on A-V differences still has to be reconciled satisfactorily. John R. Brobeck discusses some of the difficulties in the glucostatic theory and also covers the neural regulation of food intake. An integration of the current views is given by Morton I. Grossman.

Since some of the clinical aspects of regulation are also included, this volume should be a valuable acquisition for physicians, dietitians, and others who are interested in basic nutritional problems.

R. VAN REEN

ADVANCES IN FOOD RESEARCH. *Volume VI.*

Edited by E. M. Mrak and G. F. Stewart. Academic Press, New York. $9.00. xii + 398 pp.; ill. 1955.

Seven extensive review articles are presented in this volume. They cover five specialized areas and two general topics, as follows: Application of Research to Problems of Candy Manufacture (L. F. Martin); Bacterial Spoilage of Wines with Special Reference to California Conditions (R. H. Vaughn); Microbiological Implications in the Handling, Slaughtering, and Dressing of Meat Animals (J. C. Ayres); Microbiological Problems of Frozen Food Products (G. Borgstrom); Potato Granules, Development and Technology of Manufacture (R. C. Olson and W. D. Harrington); The Thermal Destruction of Vitamin B_1 in Foods (K. T. H. Ferrer); and Tunnel Dehydration for Fruits and Vegetables (P. W. Kilpatrick, E. Lowe, and L. B. Van Arsdel).

As in previous volumes, the editors have chosen topics which will be of considerable interest to processors, manufacturers, and food technologists, as well as dietitians. Because of the great detail in the presentations, the book should prove of value as a reference work in these areas.

R. VAN REEN

BIOPHYSICS AND GENERAL PHYSIOLOGY

MOLECULAR THEORY OF GASES AND LIQUIDS.

By Joseph O. Hirschfelder, Charles F. Curtiss, and R. Byron Bird; with the assistance of the staff of the University of Wisconsin Naval Research Laboratory. John Wiley & Sons, New York; Chapman & Hall, London. $20.00. xxvi + 1219 pp.; ill. 1954.

This major work represents a tremendous advance in the development of applied statistical mechanics, and is motivated by an increasing need to predict certain properties of gases under conditions not readily amenable to experimental measurement. Powerful methods have been developed which are based on empirical potential functions rather than on pure quantum mechanics. At first glance, the only connection between this book and biology would seem to be the fact that the principal author's father was a distinguished pharmacologist. However, the advances summarized here do hold out some hope for the direct application of theoretical physico-chemical considerations to complex biological systems, since the calculations necessary to predict the course of rapid combustion of a mixture of gases at a high temperature approach in complexity those which might be made to predict, e.g., the interaction of membranes and ions, beginning from purely physical and chemical considerations. On the whole, the work requires a knowledge of physics, chemistry, and mathematics far beyond any level used in biology, and the specific applications treated have no biological pertinence.

PAUL CRANEFIELD

EINFÜHRUNG IN DIE BIOLOGISCHE REGISTRIERTECHNIK.

By Herbert Klensch. Georg Thieme Verlag, Stuttgart. DM 33.–. xii + 222 pp.; ill. 1954.

This survey of recording techniques is rather well confined to physiological techniques, and the title is therefore a little misleading. Section I, The Registration of Mechanical Changes, deals with muscle levers, kymographs, optical levers, tambours, and transducers. Section II surveys the recording of volume and pressure changes in gases and liquids. Section III briefly discusses temperature recording. Section IV is devoted to electrophysiological techniques. Other topics treated include radioactivity measurements, photography, and excitation techniques. The rather long chapter on excitation, chiefly devoted to electrical excitation, is out of place in a book on recording techniques, but fits

very nicely into a book on various applications of physics to physiology, which is what this book really is. Nothing is covered in much detail but the fact that so many things are covered gives the book a certain usefulness. Unfortunately, the literature references are very largely confined to the German literature. This means they are somewhat out of date.

PAUL CRANEFIELD

BIOCHEMISTRY

EINFÜHRUNG IN DIE ENERGETIK UND KINETIK BIOLOGISCHER VORGÄNGE.

By W. Bladergroen. Wepf & Company, Basel. S. Fr. 28.–. x + 368 pp.; ill. 1955.

An introduction to the energetics and kinetics of biological phenomena. For an understanding of most books dealing with biological kinetics and energetics, a knowledge of calculus, physics, and physical chemistry is considered a prerequisite. However, while writing his book, Bladergroen has kept in mind the needs of the many biologists, medical men, and students whose background of these prerequisites is only rudimentary. He has chosen to present his subject matter as a survey of the field. The book has a concise, yet readable style and English-speaking readers will be particularly grateful for the translation (as footnotes) of some technical terms.

In this comparatively small volume, the reader first receives a thumbnail sketch of some topics in physical chemistry (pp. 1–88). Thus fortified, he can proceed to the chapters in which the physio-chemical principles are related to biological systems and problems. The entropy principle, the quantum theory, oxidation-reduction potentials, free energy changes, and reaction kinetics are discussed as applied to discrete biological entities.

The three chapters in which the author describes catalysis, biocatalysts, and enzyme kinetics contain some oversimplification and do not cover all aspects. One misleading oversimplification is the conception that enzymes *can* be classified in a satisfactory manner by relating them to the kinetics of the reaction which they "catalyze." One omission: there is no ample discussion of "active sites" on enzymes, a topic which is becoming increasingly important for an understanding of enzyme mechanisms.

In addition to a consideration of photosynthesis and chemosynthesis and a discussion of phosphate formation in biological systems. Bladergroen fittingly ends his book with chapters on food value and total energy exchange, thus relating the study of biological energetics and kinetics of isolated, in vitro systems to the animal organism as a whole.

CLAUDE F. BAXTER

RESONANCE IN ORGANIC CHEMISTRY.

By George Willard Wheland. John Wiley & Sons, New York; Chapman & Hall, London. $15.00. xiv + 846 pp.; ill. 1955.

The breadth of coverage and detail of discussion make this an outstanding book in organic chemistry. The author makes numerous analogies and considers several individual cases to expose the concepts of valence and resonance. The first two chapters, which deal with the theory of resonance and the nature of valence, can be profitably consulted by those with advanced training in organic chemistry as well as by the novice. The theme of the book, resonance, is discussed in relation to resonance energy, steric effects, dipole moments, molecular spectra, chemical equilibrium, and chemical reaction. A final chapter, for the more ambitious student is on the mathematical basis of resonance.

For the investigator who is interested in molecular configurations of naturally occurring materials the appendix presents a compilation of bond lengths and bond angles of a wide variety of compounds—about 650 in all. In the list are amino acids, dipeptides, purines, pyrimidines, a pyrimidine riboside, a disaccharide, penicillin, a cholesteryl compound, and many of the mono- and di-carboxylic acids that are metabolically important.

This book should be available to all whose interests border on fields of organic chemistry. Its wide scope as well as its data on molecular dimensions make it an excellent reference book. It will undoubtedly find its place as a textbook in advanced courses in spite of its price.

K. BRUCE JACOBSEN

PROGRESS IN STEREOCHEMISTRY. *Volume I.*

Edited by W. Klyne. Academic Press, New York; Butterworths Scientific Publications, London. $8.00. x + 378 pp.; ill. 1954.

It is somewhat difficult to decide to which group of workers in the sciences this book is specifically directed. The subjects cover a wide range of disciplines related to the field of stereochemistry. The editor strived for as little repetition in the chapters as possible, and that goal has been achieved remarkably well. However, this may as a consequence force a biochemist who is interested in a certain small item of information to go through a chapter directed to physicists. The reason seems to lie in the intention to make the book supplementary to older, existing textbooks. The result is an unfortunate hybrid between a textbook and a review book.

When a contributor has tried to give a comprehensive progress report on a given subject, a very strict summary of recent literature results, as is the case in the chapter by W. Klyne on the conformation of six-membered rings. Such a chapter is lost upon the

scientist who is only slightly initiated into the field. On the other hand, the same author collaborated in writing a very lucid chapter on the correlation of configuration, a chapter which succeeds not only in enumerating but also in explaining the new achievements in this branch of stereochemistry. Finally, there are chapters which do not comprise either a review or a comprehensive discussion of new results in a particular field. The chapter on the stereospecificity of enzymes admittedly does not attempt the monumental task of completely reviewing the literature, but the author has unnecessarily extended the scope of stereospecificity to include such subjects as the inhibition of cholinesterase and proteolytic enzymes by the organophosphorus derivatives, although that does not even correctly fall under the broader subject of substrate specificity. One may summarize by saying that this book, though each chapter has individual merit, is an unhappy combination, both in scope and manner of treatment, of the subject matter.

J. VAN EYS

THE LUMINESCENCE OF BIOLOGICAL SYSTEMS. *Proceedings of the Conference on Luminescence March 28–April 2, 1954, sponsored by the Committee on Photobiology of the National Academy of Sciences-National Research Council and Supported by the National Science Foundation.*

Edited by Frank H. Johnson. American Association for the Advancement of Science, Washington. $7.00; (AAAS Members, $6.00). xiv + 452 pp.; ill. 1955.

This book is a collection of 17 papers presented at a conference to which participants came from Holland, Japan, England, and Australia, as well as from the United States. The subjects vary from absolute reaction rates to ecology, but all have something to do with light, and include absorption, phosphorescence, luminescence, or fluorescence in a test tube or in a living organism. Some of the techniques described are particularly timely in view of the present increased interest in light absorption as well as light emission.

The first paper was presented by E. Newton Harvey. This was appropriate, since many of those present were his colleagues or first or second generation students. His contribution contains a comprehensive tabulation of luminous organisms.

The biochemistry of luminescence is discussed in a series of detailed papers on the three best characterized systems, the crustacean *Cypridina*, the firefly, and salt-water bacteria. Each system contains an enzyme "luciferase" as well as a substrate "luciferin," and each system is an oxidative process requiring oxygen and resulting in light emission. Here the similarity ends. The enzymes are not interchangeable. The partial purification of both the firefly and bacterial luciferases is reported, along with kinetic studies and proposed mechanisms of light production. The bacterial reaction requires both flavin mononucleotide and a long chain fatty aldehyde. In addition to its own luciferin (which is a fluorescent molecule partially characterized), the firefly system requires magnesium ion and adenosine triphosphate. Methods of purification and characterization of *Cypridina* luciferin are presented. It is a polypeptide with a chromophore group. These differences may be a reflection of the general oxidative mechanisms in the organisms.

The titles of some of the other papers are: Luminescence Spectroscopy . . . and the Photosynthetic System, Fluorescence Spectrophotometry, Kinetics of Chemiluminescence, Spectroscopic Investigations of Luminescent Systems, Inhibition and Activation of Intracellular Luminescence, Physiological Control of Luminescence in animals, and Luminescent Organisms of Japan and the Far East.

ARDA A. GREEN

ADVANCES IN CARBOHYDRATE CHEMISTRY. *Volume 10. Edited by M. L. Wolfrom; assistant editor, R. Stuart Tipson. Academic Press, New York.* $10.50. xx + 437 pp. + 1 pl.; text ill. 1955.

With the completion of a series of ten issues, this volume of *Advances in Carbohydrate Chemistry* comes of age. By furnishing critical and intergrading reviews throughout the years, this publication has served as an excellent medium for keeping chemists and biochemists informed about the progress in the ever-expanding subject of carbohydrate chemistry.

Volume 10 contains nine chapters on various aspects of the subject. It opens with a discussion of the Stereochemistry of Cyclic Derivatives of Carbohydrates, by J. A. Mills, in which the carbohydrates are compared with analogous alicyclic compounds, so as to emphasize the stereochemistry of the ring system. Mills hopes that the information obtained from the study of alicyclic compounds will assist in the coordination of the available information about carbohydrates and will lead to a further development of the stereochemical theory.

The second article, Column Chromatography of Sugars and their Derivatives, by W. W. Binkley, is a description and critical evaluation of the various techniques involving column chromatography of sugars.

A chapter on Glycosylamines, by G. P. Ellis and John Honeyman, discusses the chemistry of carbohydrates containing nitrogen. Its scope is limited to compounds resulting from the condensation of a reducing sugar with ammonia or of a primary or secondary aliphatic, alicyclic, or aromatic amine. The following chapter, entitled The Amadori Rearrangement, and written by J. E. Hodge, deals with the same subject, and is primarily concerned with the various stages

involved in the isomerization of an aldosylamine to a 1-amino-1-deoxy-2-ketose.

Methods of preparation and a discussion of the reactivity of the useful glycosyl halides is presented in a chapter called The Glycosyl Halides and their Derivatives by L. J. Haynes and F. H. Newth. These writers emphasize the poly-O-acyl derivatives of this class of compounds, which are among the most important intermediates for synthesis in carbohydrate chemistry and whose chemistry is of considerable intrinsic interest.

The series of chapters on methyl esters contained in earlier volumes is augmented by G. G. Maher with two articles, one on Methyl Ethers of D-Galactose. Methyl pentose and D-galactose are constituents of numerous natural polysaccharides. The methylated monosaccharide derivatives serve as reference compounds and are of utmost importance in the study of the chemical constitution of polysaccharides.

W. J. Polglase, in an article on Polysaccharides Associated with Wood Chemistry, discusses the carbohydrate composition of numerous wood-cellulose preparations, and the structure of the associated polysaccharides, such as xylan, mannan, and galactan. The current theories on the nature of the association between the various components of wood cellulose are also considered.

The volume concludes with an account of the recent developments in the Chemistry of Heparin, by A. B. Foster and A. G. Huggard. Heparin, the blood anticoagulant present in circulatory tissue, is now recognized to be an important and chemically unique polysaccharide of considerable biological significance.

Most of the chapters include extensive and useful tables summarizing the properties (specific rotation, rotation solvent, and melting point) of the classes of compounds dealt with.

The volume also contains an obituary of the late gifted carbohydrate chemist, E. G. V. Percival, who died at the early age of 43 at the height of his career.

W. Z. Hassid

Chemistry and Biology of Pteridines. *Ciba Foundation Symposium.*

Edited by G. E. W. Wolstenholme and Margaret P. Cameron. Little, Brown & Company, Boston. $8.00. xiv + 425 pp. + 10 pp.; text ill. 1955.

The Ciba Foundation Conferences and Symposia have acquired an excellent reputation in the few years since they have been initiated. *The Chemistry and Biology of the Pteridines* is another example of the Foundation's well-directed colloquia. This symposium achieved a good balance between the chemical and biological aspects of the pteridines. An additional feature was a large amount of specific practical chemical information, not usually found in publications of this sort.

Great strides in elucidating the mechanism of action of folic acid in the metabolism of one-carbon fragments have been made since this symposium was held. The only reference made here to the mechanism of formylation by tetrahydrofolic acid is in a discussion.

The conclusion of the editors that pteridines are among the most important growth activators known to man is only a mild way of expressing the truly exciting leads which are discussed in many of the papers, even to the point of renewing the hope of modifying abnormal growths with pteridine derivatives.

J. van Eys

The Systematic Identification of Organic Compounds. *A Laboratory Manual. Fourth Edition.*

By Ralph L. Shriner, Reynold C. Fuson, and David Y. Curtin. John Wiley & Sons, New York; Chapman & Hall, London. $6.00. x + 426 pp. + 2 charts; text ill. 1956.

The biochemist and cellular physiologist should find this manual an extremely interesting and valuable book to have at his elbow when problems of the molecular identification of biologically active compounds become a vital and necessary part of a research program. The text is something more than a series of methods for systematic analysis, however, and an attempt is made to give the student the necessary background for the assumption of responsibility in his own work. This is done by laying more stress on the theories which form the basis of identification rather than on the specific techniques and apparatus used in such procedures. It is, of course, necessary that familiarity with techniques and the advantages and limitations of the various tools be appreciated and understood, but this familiarity is gained through laboratory use and the testing of procedures outlined in this volume. The present edition is an improvement over earlier ones (*Q.R.B.*, 23: 173. 1948), and while specifically written for the developing organic chemist, its value to biological fields should not be overlooked.

Organic Reactions. *Volume VIII.*

Roger Adams, Editor-in-Chief. John Wiley & Sons, New York; Chapman & Hall, London. $12.00. viii + 437 pp.; ill. 1954.

Organic Reactions, a series started in 1942 with the intention of providing an authoritative compilation of all the important synthetic chemical reactions, is well known to the organic chemist and to the biochemist who is engaged in the synthesis of biologically active compounds and their analogues. Volume VIII, however, should be of more than general interest to the biologist who has only an occasional desire to synthesize some specific compound or type of compound, since the

major portion of the volume is devoted to some methods of preparation of aldehydes and ketones, with a general description of the reactions which these compounds may undergo. This information may be particularly useful when one considers that the carbonyl group, in addition to occurring frequently in natural products, can serve also as a convenient point of attack in the synthesis of a great variety of complex molecules.

Written by one or more men who have had special experience with the reaction they write about, each chapter provides a comprehensive survey of a particular reaction or type of reaction and includes a general discussion of methods, modifications, examples of applicability, special precautions, a detailed description of the procedure, expected yields, and other pertinent data. Included in each chapter are extensive tables listing compounds which have been prepared by or have been subjected to the reaction under discussion. The material presented is exceptionally well referenced and represents a rather complete survey of the pertinent original literature through 1952, with the inclusion of some more recent references.

The topics discussed in Volume VIII are the following: The Catalytic Hydrogenation of Esters to Alcohols (H. Adkins), which also describes methods for the preparation of amino alcohols and of glycols in good yield; The Synthesis of Ketones from Acid Halides and Organometallic Compounds of Magnesium, Zinc and Cadmium (D. A. Shirley), and The Sommlet Reaction (S. J. Angyl), two articles which are useful in the synthesis of steroid as well as other ketones; The Acylation of Ketones to Form β-Diketones or β-Ketoaldehydes (C. R. Hauser, F. W. Swamer, and J. T. Adams), a contribution which describes the preparation of compounds of a type widely used in the synthesis of biologically important substances; The Synthesis of Aldehydes from Carboxylic Acids (E. Mosettig), a chapter in which 7 of the most common methods are described; The Metalation Reaction with Organolithium Compounds (H. Gilman), which describes intermediates that make possible the convenient preparation of many products not readily available through other routes; Beta-Lactones (H. E. Zaugg), a chapter describing the preparation of compounds which sometimes offer a stereo-specific synthetic route; and finally, The Reaction of Diazomethane and its Derivatives with Aldehydes and Ketones (C. D. Gutsche).

ENNIS LAYNE

ORGANIC SYNTHESES. *An Annual Publication of Satisfactory Methods for the Preparation of Organic Chemicals. Volume 34.*

William S. Johnson, Editor-in-Chief. John Wiley & Sons, New York; Chapman & Hall, London. $3.50. vi + 121 pp.; ill. 1954.

Organic Synthesis, an annual publication of tested methods for the preparation of organic compounds, is a valuable compilation for the biochemist who is engaged or interested in the synthesis of biologically active compounds or analogues. Volume 34 offers confirmed methods for the preparation of 33 organic chemicals.

ENNIS LAYNE

ORGANIC SYNTHESES. *An Annual Publication of Satisfactory Methods for the Preparation of Organic Chemicals. Volume 35.*

T. L. Cairns, Editor-in-Chief. John Wiley & Sons, New York; Chapman & Hall, London. $3.75. vi + 122 pp.; ill. 1955.

Volume 35 of *Organic Synthesis* contains tested methods for the preparation of 36 organic compounds. Among these, three methods for the conversion of cholesterol to its ketonic and isomeric unsaturated derivatives are offered. These might make a valuable addition to the general biochemical laboratory curriculum as a practicable, economical, and reproducible means of acquainting the student with some aspects of steroid chemistry.

ENNIS LAYNE

COLE'S PRACTICAL PHYSIOLOGICAL CHEMISTRY. *Tenth Edition.*

Revised and re-written by Ernest Baldwin and David James Bell. W. Heffer & Sons, Cambridge. 21s. x + 261 + ii pp.; ill. 1955.

This small text is designed to serve as a laboratory manual for a course in physiological chemistry in the medical curriculum at Cambridge. Much of the framework and of the philosophy of the previous edition, published twenty years ago, has been retained. The emphasis is on experiments that can be performed with a minimum of time and of equipment and with a maximum of satisfactory results in the hands of medical students.

The organization of the book is conventional. The first chapters introduce elementary concepts of physical chemistry, such as *p*H and the properties of solutions. These are followed by classical experiments on proteins, fats, and carbohydrates. The chemistry of foods and of digestive processes is covered briefly. The remainder of the book describes qualitative and quantitative analytical procedures for certain constituents of blood and urine. There is included an experiment on the effect of dietary changes on the urinary excretion of various nitrogenous end-products.

Little criticism can be made of most of the material presented. It would have been preferable to use more modern terminology in the physical chemistry section and to express concentrations of electrolytes as millimoles or milliequivalents per liter rather than as milligrams per cent. In addition, inclusion of an experiment on the determination of the carbon dioxide content of serum and of experiments on electrophoretic and

chromatographic separations should have been possible within the framework of such a course. Because of these omissions, the usefulness of the book is limited. It does not provide an adequate preparation for the understanding and management of the acid-base, electrolyte, and metabolic disorders encountered on hospital wards.

F. P. CHINARD

NEUROCHEMISTRY. *Progress in Neurobiology: 1. Edited by Saul R. Korey and John 1. Nurnberger; 23 contributors. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York.* $6.75. xii + 244 pp.; ill. 1956.

This volume in *Progress in Neurobiology* includes 16 articles which range into many areas loosely associated with neurochemistry. Though published this year, the symposium which the book reports apparently occurred in 1954, although this for some reason is not clearly specified. The topics presented are the following: the separation of sphingosine and related compounds (J. B. Wittenberg); γ-aminobutyric acid (E. Roberts); enzymatic thioltransacetylation (R. O. Brady and E. R. Stadtman); brain copper proteins (H. Porter and J. Folch-Pi); the relation of ceruloplasmin and plasma copper to hepatolenticular degeneration (I. H. Scheinberg); structure and function in the neuron (S. L. Palay); adaptive enzyme formation in morphogenesis (M. W. Gordon); chemical changes in the postnatal development of rat brain (W. K. Jordan, R. March, and R. A. Messing); the structure of ribonucleic acid (A. Rich); the effects of brief stress on the ribonucleic acid and labile nitrogen pool of rat brain and liver (J. L. Nurnberger and M. W. Gordon); studies on acetal phospholipids (S. R. Korey); the action of tertiary and quaternary nitrogen derivatives upon the acetylcholine acceptor (I. B. Wilson and M. Altamirano); the neurochemistry of seizures (D. B. Tower); the chemistry of brain lipoproteins and allergic meningoencephalomyelitis (N. P. Goldstein and M. W. Kies); the relation of cerebral circulation and metabolism to mental activity (L. Sokoloff); and cerebral metabolic rate in children (C. Kennedy). Although the bibliographies are seldom extensive, references to recent reviews are frequent. Several of the contributions consist of reports of current research, while others (those by Roberts, Brady and Stadtman, Palay, Rich, Wilson and Altamirano, and Tower) took the form of more general discussions and reviews. These provide a very useful survey of the field. A somewhat related symposium in which a number of the above authors participated may interest the reader: *Biochemistry of the Developing Nervous System* (edited by H. Waelsch, Academic Press, 1955).

The average length of each contribution is 16 pages, and there is almost no overlapping of subject matter. The next two proposed volumes in the present series will report on the ultramicroscopic morphology and cytochemistry of the nervous system and on psychopharmacology.

As one reads of the efforts to understand the chemistry of the nervous system, an appreciation for the task of opening up a new area of investigation soon develops. It is unfortunate that such a lag occurred in the publication of this information, since the area is developing so rapidly. A recently published textbook now embodies much of the background material as well as new information in the field of neurochemistry. It is *Biochemistry and the Central Nervous System*, by H. McIlwain (Little, Brown and Co., 1955).

K. BRUCE JACOBSON

HEALTH AND DISEASE

THE HISTORY AND CONQUEST OF COMMON DISEASES. *Edited by Walter R. Bett. University of Oklahoma Press, Norman.* $4.00. x + 334 pp. 1954.

Bett's earlier work, *A Short History of Some Common Diseases*, was a minor classic and is now a rather hard to find, out of print item, so this new version is very welcome. It is, as the editor points out, an entirely new book, with new contributors. The chapters and contributors are as follows: Acute Communicable Diseases (George Rosen); Influenza (C. H. Stuart-Harris); Pneumonia (E. M. and William Brockbank); Tuberculosis (Lewis J. Moorman); Rheumatism (W. S. C. Copeman); Arthritis (Edward F. Hartung); Heart Disease (Terence East); Bright's Disease (Ralph H. Major); Tonsils and Adenoids (R. Scott Stevenson); The Venereal Diseases (Douglas J. Campbell); Rickets (A. White Franklin); Diseases of the Endocrine Glands (A. P. Cawadias); Gallstones (Donald C. Balfour); Appendicitis (Walter R. Bett); Epilepsy (William G. Lennox); Cancer (Harold Burrows); and Malingering (Edward L. Murphy). There is a glossary for non-medical readers and there are excellent author and subject indices. The general approach of the authors includes the history of the recognition of the disease in question as a specific entity, the development of methods of diagnosis, the history of its therapy, and a discussion of the waxing or waning incidence of the disease over the centuries. This book is useful, interesting, scholarly, well produced and inexpensive—a singularly gratifying combination.

PAUL CRANEFIELD

CANCER CELLS. *By E. V. Cowdry. W. B. Saunders Company, Philadelphia and London.* $16.00. xvi + 677 pp.; ill. 1955.

The author of *Cancer Cells* is director of the Wernse Cancer Research Laboratory of Washington Uni-

versity in St. Louis. He has spent many years in the study of changes induced in the epidermal cells of mice by chemical carcinogens, but his versatile competence in biology is indicated by outstanding contributions in general cytology and histology, and to problems of ageing as well as those of neoplasia. The title of the book fails to convey an idea of its scope, for it presents an excellent review of virtually every aspect of current knowledge about cancer.

The first four chapters describe the pattern of growth and the cytological characteristics of malignant tumors. These are followed by a chapter on the chemical properties of cancerous tissues. A chapter discussing the occurrence of cancer in plants and animals should prove of particular interest to the general biologist. The etiology of cancer is thoroughly considered in several chapters that deal with the various physical, chemical, and biological agents in turn. The roles of somatic mutation, of genetic susceptibility, and of age and sex in the development of neoplasms are ably reviewed.

Chapters on prevention, diagnosis, and treatment will be of interest to the biologist who may wish to integrate his knowledge of abnormal cell growth with the "practical" problems presented by cancer as a disease of man. The final chapter, on cancer research, provides an interesting summary of historical and contemporary work in the field. The author's personal opinions, which he freely expresses throughout the book, are here particularly evident. It is refreshing in a book of this kind to find the personal pronoun in frequent use.

A 70-page bibliography completes this well-written, well-illustrated, and well-printed book. It is highly recommended to the general biologist seeking a one-volume orientation in the field of neoplasia.

HANS G. SCHLUMBERGER

DIAGNOSTIC CYTOLOGIQUE DU CANCER GENITAL CHEZ LA FEMME.

By Raymond Bourg, Claude Gompel, and Jean-Paul Pundel; preface by Charles Oberling. Masson & Cie., Paris; Editions Desoer, Liège. 4,800 fr. xiv + 183 pp. + 84 pl.; text ill. 1954.

This book is the first French work on the subject of exfoliative cytology. The latter can be defined as the microscopic examination of cells in stained smears obtained from various body orifices. Abnormal elements which may represent cancer cells are the chief object of search in the study of these smears. Although of some use in detection of bronchogenic, gastric, and prostatic carcinoma, its outstanding value is in the early discovery of cancer of the cervix—the most common cancer of women.

The diagnosis of cancer based on the appearance of single cells in smears is fraught with considerable hazard. This book, with 83 plates, of which 30 are in color, should prove of value to the pathologist in the interpretation of questionable cells. The authors place considerable emphasis on the appearance of abnormal cells that are *not* cancerous—a very important caution indeed, for a false positive diagnosis may have sequelae as harmful to the patient as a false negative report.

The book will probably be of little interest to the general biologist or cytologist. English-reading pathologists will prefer to use *The Atlas of Exfoliative Cytology* by George N. Papanicolaou.

HANS G. SCHLUMBERGER

MEDICAL AND PUBLIC HEALTH LABORATORY METHODS. *Successor to Fifth Edition of Laboratory Methods of the United States Army.*

Edited by James Stevens Simmons and Gleon J. Gentzkow. Lea & Febiger, Philadelphia. $18.50. 1191 pp. + 9 pl.; text ill. 1955.

For many years *Laboratory Methods of the United States Army* has been a trusted reference book in many laboratories. Even at the time of the previous edition that title was no longer adequate, since its usefulness far exceeded the need of Army and even public health laboratories. A book of this sort is necessarily restricted to a few alternative methods. The book therefore serves its purpose best in situations where the relative merits of different methods are not directly under consideration, as for instance for use by technical laboratory personnel and scientists and medical men who are in need of some method outside their own fields of specialization.

The majority of the chapters are written with clarity and contain a commendable amount of elementary theory. The correlation of the parts of different contributors is not always perfect. As an example, the description of fluorometry has been purposely deleted because of the relative rarity of application, yet several methods are described which call for the use of a fluorometer. However, such imperfections are relatively insignificant and make little difference in the over-all usefulness of the book. The one chapter which reflects the original aim of the previous editions is the chapter on the analysis of foods of animal origin. This chapter reflects solely the needs of army laboratories. All the other chapters—on clinical pathology, chemical analysis of urine, blood, and waste materials, and the various parasitological sections—are perfectly general in scope.

J. VAN EYS

TEXTBOOK OF OCCUPATIONAL THERAPY, *with Chief Reference to Psychological Medicine.*

By Eamon N. M. O'Sullivan. Philosophical Library, New York. $10.00. x + 319 pp. + 1 folded chart; ill. 1955.

PSYCHOTHERAPY AND COUNSELING. *Ann. N. Y. Acad. Sci., Vol. 63, Art. 3.*

Edited by Roy Waldo Miner. New York Academy of Sciences, New York. $3.50 (paper). Pp. 319–432; ill. 1955.

PSYCHOLOGY AND ANIMAL BEHAVIOR

MINDS AND MACHINES.

By W. Sluckin. Penguin Books, Baltimore. 50 cents (paper). 223 pp.; ill. 1954.

This is the best 50 cents worth the reviewer has seen in a long, long time. It is not merely another book on cybernetics or electronic brains, but a mature and thorough discussion of theoretical biology, physiology, psychology, and philosophy by an author who is a qualified engineer, a qualified psychologist, and one who can set down what he knows so that other people can understand it. In the Foreword, C. A. Mace has stated, and rightly, that "Anyone who wants to pick up the threads of all this talk about 'cybernetics' and 'information theory,' and who wishes to begin at the beginning, can safely be advised to start at page one of this book."

It is beyond the present scope to touch upon all the points discussed in this work, but it should be mentioned that the subject matter runs the gamut in a most reasonable and orderly fashion from Computing and Other Machines, Control and Communication, Mechanisms and Organisms, The Nervous System and Learning, to Thought Processes, Adaptive Purposeful Behavior, and the Philosophy of the Mind.

The book is so stimulating that one is tempted to discuss many of its ideas at great length, and I am only restrained from doing so by the feeling that the reader would be much better off spending his time reading the book rather than the review. It is hard to see how future classes in psychology and physiology can fail to use this most admirable little book as a basic reference. Its carefully picked bibliographic listings are most important in this regard.

R. G. GRENELL

LA CYBERNÉTIQUE. *Du Cerveau Humain aux Cerveaux Artificiels. Collection: Évolution des Sciences.*

By Paul Cossa. Masson & Cie., Paris. 525 fr. (paper). 98 pp.; ill. 1955.

This is a small and interesting treatise concerned with modern concepts of the mechanisms of action of human and "artificial" brains. The author, without any undue verbosity, traces the modern "cybernetic" movement in science to its birth. He then proceeds to describe, with clarity and brevity, the concepts of feed-back, and thus of automatic, goal-seeking devices.

The book is quite adequate as an interesting discussion of a diversity of cybernetic applications, primarily for those who have some reasonable idea at the outset of what has been going on in the field. There is a reasonable bibliography which will lead those interested to some detailed and specific discussions in particular areas. In association with other works this should serve as a useful addition to the field.

R. G. GRENELL

POLICE DRUGS.

By Jean Rolin; translated, with a foreword, by Laurence J. Bendit; with an appendix on Narcoanalysis by Edward V. Saher. Philosophical Library, New York. $4.75. x + 194 pp.; ill. 1956.

The title of this book refers to the use of such drugs as sodium pentothal and related barbiturates in psychological exploration outside the psychiatric clinic, in connection with courts of law or as police drugs. The author's thesis is that narcosis produced to obtain a confession violates the individual's right to "the sanctity of secrecy." He devotes the chief part of the book to pointing out that these drugs are not "truth serums" and that the possibility of deceit and lying does exist under the muddle of fantasies and delirium associated with the twilight zone of consciousness under narcosis. The book appears at a time when there is much interest in drugs affecting behavior. Unfortunately there is little in the text to help clarify the riddle of psychopharmacology. There is nothing of toxicologic significance in the book; the title may be misleading in that respect. The critical evaluation of narcoanalysis in the appendix may be of interest to students of the medico-legal problems associated with the use of drugs in obtaining a confession.

C. JELLEFF CARR

SPEECH. *Code, Meaning, and Communication. McGraw-Hill Series in Speech.*

By John W. Black and Wilbur E. Moore. McGraw-Hill Book Company, New York, Toronto, and London. $4.50. viii + 430 pp.; ill. 1955.

This is a textbook designed to introduce the student to himself through analysis of the ways and means of expressing himself in speech. As a textbook should be, it is quite all-embracing. It represents the main currents of mid-twentieth-century thought in the field, superimposed on the tenets of the ancient academic Trivium. The book is clear and purposeful, and should prove useful in the introductory college course labelled "Fundamentals of Speech."

The dual purpose of the book, stated in the authors' "overview" of the field, is to "sketch some of the facts that are known about speech and to suggest ways and

means by which you should be able to make your own speech more effective than it is." The course of this discussion ranges from elementary physiology and psychology, through Korzybskian semantics, to rhetoric and common-sense about the communication of ideas and the creation of impressions. It is a practical book with no pretense of scholarly demonstration. It is freely sprinkled with classical quotations, and each chapter concludes with an appropriate set of exercises and assignments.

Inasmuch as a lack of critical experience in the fundamentals of careful talking, writing, reading, and thinking is a common situation of the student in the first year of college, this book will supply an adequate stimulus for his innate desire to know and use his most distinctively human attribute—the ability to use audible and visible symbols in a meaningful fashion.

WILLIAM G. HARDY

STUTTERING IN CHILDREN AND ADULTS. *Thirty Years of Research at the University of Iowa.* *Edited by Wendell Johnson; assisted by Ralph R. Leutenegger. University of Minnesota Press, Minneapolis.* $5.00. xviii + 472 pp.; ill. 1955.

As the subtitle suggests, this book is a distillation of thirty years of research at the University of Iowa on stuttering. The editor, whose personality as researcher, teacher, and advisor permeates the Iowa Speech Clinic, provides a setting for more than 40 hitherto unpublished papers. Many of these were M.A. theses; others are early papers by past and present members of the staff. All have been carefully revised or abstracted, in the interest of space and coherence, to provide a picture of "the scientific exploration of stuttering" at the University of Iowa.

As a matter of course a wide range of topics is covered, including most of what are now the basic concepts of stuttering, which "consists of the reactions made by the stutterer in an effort not to stutter." In the historical treatment, special attention is directed to "the moment of stuttering" and to observations of adaptation, consistency, and "the spontaneous recovery of the stuttering response." The core of the idea of stuttering, from the perspective of the group at Iowa, is that one is prompted "to regard stuttering as learned behavior, and to investigate it, theorize about it, and treat it clinically, as such."

For the researcher or the clinician, this idea is refreshing and useful. It represents considerable progress in thought since the reported use of a mouthful of pebbles by Demosthenes, and the lingual surgery of the early nineteenth century. Stuttering is a malicious communicative disorder. The literature on it would fill a sizeable library, and the range of theory to explain it includes most schools of thought on human behavior. It—the fact of stuttering—remains one of the serious disablers of men, and accounts for millions of lost man-hours from productive work and immeasurable losses in human happiness and achievement. A major contribution of the group at Iowa, through thirty years of inquiry, is the delineation of stuttering as a form of behavior to be observed, measured, considered, and treated; in short, to subject this aspect of human behavior to scientific method, to rescue it from the milieu of folklore, and to develop clinical techniques which are consistent with theory and laboratory findings.

The book does not solve the problem of stuttering, but it is a valuable contribution to the field. As usual, Johnson's style as writer and editor is lucid and convincing. Acquaintance with this condensation of many years of study of the problem of stuttering will furnish a good orientation to the beginning student, welcome refreshment to the advanced student, and a valuable catalyst to the convinced clinician, whatever his bent.

WILLIAM G. HARDY

HUMAN BIOLOGY

THE DISTRIBUTION OF THE HUMAN BLOOD GROUPS. *By A. E. Mourant. Charles C Thomas, Springfield, Ill.* $8.75. xxiv + 438 pp. + 9 folded maps; ill. 1954.

Human geneticists and physical anthropologists have awaited this book with the keenest expectancy, since the voluminous data being obtained about the distribution of the blood groups in human populations has not been collected in manageable form since 1939, when W. C. Boyd prepared an extensive series of tables summarizing all reports to that date. Moreover, Mourant has taken such a position of leadership in the subject that one could be quite certain that when the book appeared it would be stimulating and authoritative.

The book itself will be an indispensable reference to all workers in the blood group field for many years to come, although so rapid is the progress of surveying the blood group distributions in various new populations that the book will require frequent revision or supplementation—indeed, it already does. The scope of the work, and the enormous magnitude encompassed, is quickly revealed by the length of the bibliography—1,716 items, running in three alphabetical series because of the flood of new papers appearing while the compilation was going on. This bibliography is obviously an invaluable part of the book, and all workers in the field will be profoundly grateful to Mourant and his assistants for preparing it.

A second feature of the book that makes it an outstanding reference work is its set of tables. There are 27 major tables at the end of the book, many of them so lengthy that they had to be printed on folded pages. They cover the previously unassembled data (from

1939) on the ABO, MN and MNSs, P, Rh, Lutheran, Kell, Lewis, Duffy, and Kidd blood groups, and sickle-cell trait. The data are arranged geographically, and for a vast number of frequencies Mourant has calculated gene or chromosome frequencies by the laborious but superior method of maximum likelihood. Like the bibliography, these tables represent a contribution to blood group work of superlative value.

The text itself is all too brief (239 pages), and may warrant a mild sense of disappointment. This arises in part because of the necessity felt by the author to press the book to completion before being overwhelmed by a fresh flood of blood group data, and in part because of the still inadequate, patchy coverage of world populations by blood group studies. One cannot cavil at what is set down in these chapters, but one is left with the feeling that even the major outlines of the distributions remain obscure, partly because of the gaps in our knowledge, but also partly because of the great difficulty of making sense out of what data we already have. The book, at its present stage of development, is therefore far more significant as a working reference than as a comprehensive, not to say definitive, view of physical anthropology as seen by the blood group worker. No one realizes this better than Mourant himself, and we may fully expect to have from him when the time is ripe a sharper, world-wide picture just as clear in its outlines as already certain features of Celtic, Basque, Western European, and African distributions are becoming, thanks to the labors of Mourant himself and his colleagues.

Chapters 1–6 present the genetics, serology, and anthropological applications of the several blood group systems. Chapter 7 discusses other genetical characters of anthropological value, in what is certain to be a very stimulating vein. Chapters 8–13 take up the features of the distributions by geographic areas—Northern and Central Europe, the Mediterranean area, Africa south of the Sahara, Asia, Indonesia and Australasia, and the American aborigines. Chapter 14 touches lightly on the use of blood group distributions in studying the dynamic shifts of migrant and hybrid populations. Much more might have been said in regard to the developing importance of this field of study. A chapter on blood grouping of bone and tissue specimens is followed by one on the blood groups of animals and their relation to those of man. This is an extremely valuable summary. Chapter 17 is entitled An Attempt at a Synthesis. It is certain to stimulate much new work, for Mourant clearly points out the gaps in our present knowledge and the nature of the problems to be solved. Chapters on the Collection, Preservation, and Transport of Samples and on Gene Frequency Calculation are important for reference purposes. There is a final chapter called Some Recent Discoveries which bears witness to the speed with which the study of blood group frequencies is moving.

It is impossible to conclude without a mention of the delightfully appropriate and humorous quotations at the head of each chapter. A typically British touch—no American would dare to depart so far from our stuffy traditions of what is considered to be "scientific style." Perhaps most appropriate of all these quotations is the one which heads the chapter on the blood grouping of bone: "Our bones are dried and our hope is lost. (Ezekiel 37: 11)." It might be applied to most scientific writing, but not, you may be quite sure, to that of A. E. Mourant.

BENTLEY GLASS

A STUDY OF ABORTION IN PRIMITIVE SOCIETIES. *A Typological, Distributional, and Dynamic Analysis of the Prevention of Birth in 400 Preindustrial Societies.* *By George Devereux. The Julian Press, New York.* $6.50. xii + 394 pp. 1955.

The purpose of this study is set forth clearly in the Foreword: "(1) To develop a typology of practices and attitudes pertaining to abortion . . . as a means of providing an objective proof for the . . . axiom that cultural diversity demonstrates the tremendous plasticity and variability of human behavior. (2) To provide . . . an empirical basis for two major theorems: (a) *The methodological thesis* that the intensive analysis of the context and implications of a particular institution in a single tribe or of the still proverbial Viennese neurotics can . . . yield universally valid conclusions, and that the selfsame propositions could also be derived from a study in breadth of the variations of the same culture-trait or institution in a large number of societies. . . . The chief merit of this methodological thesis seems to be that it justifies simultaneously, and by identical means, both studies in depth and studies in breadth. (b) *The substantive thesis* that, were anthropologists to draw up a complete list of all known types of cultural behavior, this list would overlap . . . with a similarly complete list of impulses, wishes, fantasies, etc., obtained by psychoanalysts in a clinical setting, thus demonstrating . . . the psychic unity of mankind and the validity of psychoanalytic interpretations of culture. . . . (3) To present . . . source material on the topic under investigation, so as to enable future workers, as well as critics, to carry further and to correct, whenever necessary . . . the implications and conclusions of the present work."

There will probably be a consensus among readers that Devereux has admirably succeeded in the first and third of his major objectives. These accomplishments alone will secure his work a place in the history of research and the attention of scholars in a broad range of fields. Whether he will be considered equally successful in his second objective will depend, to a considerable degree, on the reader's ability to accept the concepts and the mental discipline of psychoanalysis. In the absence of such acceptance, a large portion of

the author's argument will leave many readers unconvinced.

CHRISTOPHER TIETZE

BIOMETRY

THE ELEMENTS OF PROBABILITY THEORY *and Some of Its Applications.*

By Harald Cramér. John Wiley & Sons, New York; Almqvist & Wiksell, Stockholm. $7.00. 281 pp.; ill. 1955.

Cramér's textbook has been rather well known and well thought of for some time. It is now presented by John Wiley & Sons as another volume in their series on statistics. Cramér's style has a certain dry precision and lucidity which appeals to the reviewer. His approach is primarily mathematical. Although a knowledge of calculus might fulfill the formal prerequisite for using this book, a certain level of mathematical sophistication is assumed, a level not reached in an ordinary calculus course in this country. The material covered is, however, not markedly different from that covered in the usual third-year college course in probability: normal distributions in one and more dimensions, chi square, t and F distributions and applications to sampling and inference. The emphasis is on laying a background for statistical applications. In some respects the over-all content of the book is not congruous with the style: the mathematics is mature but classical, and therefore places rather higher demands on the non-mathematician than he is likely to be able to meet, whereas the approach is not modern enough to appeal to the undergraduate mathematician (for example, generating functions are not used). This is consequently a book which will appeal to those scientists whose mathematics is sound but not modern. Accepted in those terms, it is extremely satisfying.

PAUL CRANEFIELD

FACTORIAL ANALYSIS *for Non-Mathematicians.*

By C. J. Adcock. Melbourne University Press, Carlton, Victoria; [Cambridge University Press, New York]. $3.00. 88 pp.; ill. 1954.

This little volume has the commendable aim of attempting to enable the student to get a quick insight into what is involved in factor analysis without laboring through any mathematical equations. The author states that "the present book sets out to cover the essential processes of factor analysis in such a way as to make clear the underlying logic in simple language. To the mathematician it may seem clumsy and ineffective, but neatness of mathematical statement is no help to those not schooled in its use. The basic processes are sufficiently simple, and there is no reason why students with the most elementary mathematical background should not sufficiently understand them to make some use of them in research and to be critically appreciative of research done by others." The book should be of value as introductory orientation, and in helping to bridge the gap between the experts and those who may distrust a technique which is becoming more and more esoteric.

EVELYN HOWARD

DE OMNIBUS REBUS ET QUIBUSDAM ALIIS

A SOURCE-BOOK OF BIOLOGICAL NAMES AND TERMS. *Third Edition.*

By Edmund C. Jaeger; illustrations by Merle Gish and the Author. $5.75. xxxvi + 317 pp.; ill. 1955.

Those who are not familiar with the two earlier editions of this book will find it a mine of information on the meaning and derivation of biological words. The origin and original intent of some 12,000 elements of biological jargon are given, so that the coverage is extensive, indeed; but it should be pointed out that this is not a dictionary in the usual sense, since its emphasis is principally etymological. Also included are brief biographies of those who have been honored by having their names added to the biological language in the form of generic and specific designations. An added appendix of some 1000 new terms makes this a distinct improvement over earlier editions.

C. P. SWANSON

THE VOLCANIC ROCKS OF THE ROSS ARCHIPELAGO. *British Antarctic ("Terra Nova") Expedition, 1910, Natural History Report. Geology. Vol. II, No. 1.*

By W. Campbell Smith. British Museum (Natural History), London. £3. (paper). 107 pp. + 6 pl., 2 maps; ill. 1954.

THE QUARTERLY REVIEW OF BIOLOGY publishes critical reviews of recent researches in all of the special fields of biological science. The contribution should present a synthesis or digest of the researches and a critical evaluation of them. A mere synopsis of the literature without evaluation or synthesis is not desirable.

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Material ordinarily taking the form of footnotes is set in small print and placed in the text and consequently should be written in a style so as to fit readily into the text. Acknowledgments are printed in the text in small type at the end of the article just preceding the List of Literature. Recent issues of the Quarterly should be examined for style as regards (1) section or subsection headings in the text, (2) literature citations in the text, and (3) List of Literature.

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A feature of the REVIEW is the section dealing with *New Biological Books*. In this department the book literature of different countries in the field of Biology is given prompt notice.

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